Original Communications

AMERICAN GYNECOLOGICAL SOCIETY*

FORTY-EIGHTH ANNUAL MEETING

PRESIDENT'S ADDRESS

By JOSEPH BRETTAUER, M.D., NEW YORK, N. Y.

THE privilege of addressing this meeting as its president is one which I appreciate deeply. Will you allow me to express to you my sincere thanks for this honor, as unexpected as it was undeserved?

Presidential addresses offer extraordinary opportunities; one is not confined to consideration of professional matters or to science, but may admonish, philosophize or air pet theories; in short, talk about anything if only it is brief.

My predecessors have in their annual addresses fully covered the ground of our achievements and failures, our hopes and ambitions. An organization of forward looking men has been built up, strengthened from time to time by additions from the younger group, eager to do honor to our profession, and turning often from the beaten path to original and fruitful lines of endeavor.

My subject today, *A Point of View*, is strictly speaking not a medical one, but one with which we gynecologists may well concern ourselves. This point of view has to do with the famous one of Sir William Osler concerning age and mental activity, which has had such an enormous influence. I have in mind his idea of the crisis supposed to occur in individuals at the age of forty, not the misinterpretation of his statement concerning men of sixty. He believed that about the age of forty, a definite change takes place in the human mind, with

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an actual loss in mental capacity, in consequence of which the performance of any new or creative function is not possible. The general widespread belief (which is often justified) is that middle-aged people are not qualified to undertake new jobs; that as a rule they are set in their ways and lack the ability to change their habits.

It is this point of view that I want to challenge. I want to show the value of the opposite concept, with its bearing upon the lives and problems of men and women.

The human mind has two functions, memory and the ability to reason. Every other mental activity depends upon these two functions. So-called original thinking is only the use of these along selected lines. Learning by rote is easier in youth because memory is then at its best, but real learning is the result of experience and the power to reason, and both of these increase with age. Let us grant that memory may, and frequently does, become weaker with age; the rôle played by memory, however, has become less and less important with the lapse of time. In Dante's day it was possible for one man to know everything, but the known facts in the world today are so overwhelming in number that no one man can know them all. Thus from the point of capacity, there is no valid reason why the human mind after the fortieth year should not function as well if not better than before.

There are many examples of great mental activity late in life; Cato learned Greek at eighty; Pasteur did his epoch making work after fifty; Michelangelo did his magnum opus at the age of ninety; Goethe finished *Faust* at eighty; the telescope was invented by Galileo in his seventy-third year; Titian painted one of his most celebrated pictures, ''The Battle of Lepanto,'' at ninety-eight; Oliver Wendell Holmes is today at eighty-seven one of the most active members of our Supreme Court; Weir Mitchell turned to successful literary work after seventy, and Foch, Generalissimo of the Allies, at seventy conceived and executed the strategic movements which brought the World War to a close.

Could the ordinary man do these things? Are all these men exceptions? A closer study of their lives and of the impetus and influence which stimulated them to these achievements is necessary before it can be said that they *are* exceptions.

Osler was a keen observer and he saw that the average man does cease to progress after forty. It appears to me, however, that while he was right as to the occurrence of this stasis in the average individual, the examples that can be cited of accomplishment late in life, and the analysis made of the functions of the human mind, show that the reasons for this occurrence are not what he thought they were.

If we consider the factors in the life of the average man, another possible explanation can be found. Up to the age of forty or there-

about, the average individual is occupied with earning a livelihood; almost everything he does is subordinated to this main end, with the result that when he reaches the age of forty, his habits of life are fixed and he has come to think, day by day, in a stereotyped way. He regards himself as middle-aged, as settled, and expects little change in the course of his future life. Without some unusual stimulus the habits of thought and mode of life thus acquired will not change; it is the unusual stimulus which creates the exception. Whatever the nature of the stimulus may be, we may assuredly say that the point of view which makes a man believe that he is old and settled at forty is *not* an impetus to further development; but the idea that growth and development of the mind right on through life is not only possible, but has taken place repeatedly, is on the other hand a powerful impetus to future progress. I believe firmly that if this were generally recognized, we would see the average person accomplishing to a far greater degree that which now seems possible only for the exceptional individual. We as physicians can do much to promote this idea.

If the law of ratio of adolescence and duration of life holds true, and if the elephant who matures at forty lives to the age of two hundred, and the dog maturing in two years lives to the age of ten, then man who matures at the age of twenty should live to the age of one hundred. We have not, however, achieved this biologic standard; perhaps we have in some way degenerated physically, although this is not supported by statistics. About the year 1600 the expectancy of life was between twenty-five and thirty years; at the end of the last century it was from forty-two to forty-four years, and now statistics show it to be fifty-seven years. Now as between a possible one hundred and the actual fifty-seven, let us take as a working scheme the Biblical three score and ten. If instead of believing that we cease to progress at forty, we realize that after this age we may have the optimum period for mental growth and achievement, is it not reasonable to suppose that many of the unfulfilled dreams and possibilities of the average individual can and will be developed?

This outlook is of special importance to women, and so may be considered a matter of interest to us as gynecologists. Up to recent times woman was concerned entirely with domestic and social duties. Our mothers and grandmothers married young, kept house, and brought up their children; at forty their work was finished; they sat down by the fireside and were old. Within the last few decades great changes have taken place; with the political, economic, and educational freedom of women, the world is open to them. The family is no longer the only and absorbing interest in their lives; it has become fashionable to have a career. The difficulties encountered are many. The care of a family takes much time and attention, so does the profession or business. Those who try to do both sooner or later (usually

sooner) fall by the wayside and form the gross of the busy practitioner's clientele. It is apparent that one or the other must be neglected.

How can women combine the care of home and children with an active life outside the home and do justice to both? In view of the possibilities of mental development later in life, the solution becomes less difficult. A woman who marries young may look forward after her family is established to a period of twenty or thirty years when she will have considerable leisure, when her mind and capacity will be at their best, and when she can become expert along whatever line her natural bent may lead her. Looking forward to this period in her life, she can try to discover as early as possible, even while conscientiously devoting herself to her family, in which direction this bent lies, and by any available means carry the thread of her interest through the decades of her domestic life so that she will be prepared for the time when she will have leisure to intensify her work.

We have all observed the fate of the woman whose children are grown up and no longer need her, and who has no other training than her domestic one. Her job is gone, leaving her full of undirected energy, her nervous equilibrium in need of support and the remainder of her life empty. So often we find at the bottom of the trouble maladjustment in her scheme of life and an unsatisfactory use of her energies.

I believe that by fostering the idea that life after forty is the ideal time for full development of the individual, that many of these capable women will be benefited and that some of our problems will be solved. We gynecologists, with the authority of our profession, can do as much if not more than the educators to advance this point of view.

ENDOMETRIOSIS FOLLOWING SALPINGECTOMY

By John A. Sampson, M.D., Albany, N. Y.

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THE name, endometriosis, was used by me[1] to indicate conditions arising from both misplaced uterine and tubal mucosa, even though I realized that it was not strictly correct in the latter. At the time it was stated that müllerianosis would be an inclusive and a correct term. Unfortunately, it suggests an embryonic origin, does not specify its derivation from mucosa and is not as descriptive as endometriosis. Objections were made to the names, endometrioma and müllerianoma, given by Blair Bell[2] and Bailey[3] respectively, because it did not seem to me that these lesions could be classified as true neoplasms. The invasion of the uterine wall by its mucosa is an excellent example of an endometriosis, but this name could not correctly be applied to the conditions resulting from the invasion of the tubal wall by its mucosa. Endosalpingiosis would be correct in the latter. The same confusion arises in the nomenclature of the implantation-like lesions of müllerian mucosa involving the peritoneum, because there is strong circumstantial evidence indicating their origin from both uterine and tubal mucosa. In my earlier studies of peritoneal endometriosis, I thought that one could often determine whether given misplaced endometrium-like tissue was of uterine or tubal origin. If it had the histologic structure of the glandular elements of a direct endometriosis, it was of uterine origin; if that of a direct endosalpingiosis, it was of tubal origin. Later studies convinced me that misplaced endometrial tissue, at times, may simulate tubal mucosa and misplaced endosalpingeal tissue may simulate uterine mucosa, so that the source of the glandular elements in these lesions cannot with certainty be determined by their histologic structure.

The incidence of endometrium-like tissue in the abdominal scar after cesarean section was utilized by me[4] to support the theory that peritoneal endometriosis, at times, might arise from the implantation of bits of uterine mucosa escaping into the peritoneal cavity. In the discussion of this paper, Cullen[5] reported three cases of postoperative endometriosis of the abdominal scar and he expressed his belief that they arose from endometrial tissue transplanted by the surgeon.

In more recent years several cases of endometrium-like tissue in abdominal scars have been reported and many of these followed operations where the uterine cavity had not been incised. These cases have influenced the supporters of the serosal theory of the origin of perito-

neal endometriosis to claim that the endometrium-like tissue of lapa-
rotomy scars arises from the inclusion of bits of the peritoneal serosa
in the wound and its subsequent transformation into müllerian mu-
cosa rather than from the growth of bits of müllerian mucosa trans-
planted by the surgeon.

Nicholson[6] has recently written an excellent paper, *Endometrial
Tumors of Laparotomy Scars*, supporting this theory. He has carefully
studied the principal cases which he found in the literature and has
given abstracts of these. They include those reported by Meyer,
Klages, von Franqué, Fraas, Cullen, Mahle and McCarty, Lauche,
Tobler, Lochrane, Lemon and Mahle, Rosenstein and one of his own.

He groups these cases according to the nature and purpose of the
original operation, as follows:

1. Ventrofixation of the uterus, fifteen cases.
2. Operations for perforation or rupture of the pregnant uterus, two cases.
3. Hysterectomy, one case.
4. Operations on the fallopian tubes or ovaries without hysterectomy, six cases.
5. Operations on the uterine ligaments, one case.
6. Appendicectomy, two cases.
7. Abdominal incision and drainage of suppuration in the pelvis, one case.

The anatomic continuity between the epithelium of the uterine mu-
cosa and that of the tumor of the abdominal wall was not established
in a single instance in the cases collected by Nicholson. He states
that these tumors may be explained with the help of one of three theo-
ries. "It is assumed that the tumor arises either in a cell rest which
was displaced in development or in a fragment of endometrium dis-
placed in adult life or by proliferation and changes of type of epi-
thelial cells of the peritoneum."

He concludes that

"1. Endometrial tumors are acquired accessory uteri.

"2. Of the theories which attempt to explain them the 'peritoneal'
is the most generally applicable and its acceptance offers the fewest
difficulties. It alone agrees with biological facts."

Novak[7] questions the origin of the endometrial tissue in abdominal
scars by transplantation. He mentions a case reported by Pankow
where such a condition developed in the abdominal scar of a woman
at the age of thirty, following the removal of the appendix when she
was a child. He reports a case of his own containing typical endome-
trium following the removal of one tube and ovary. He does not be-
lieve that there is sufficient evidence for assuming that these cicatrix
endometriomas are due to the actual transplantation of endometrial
tissue, especially in cases where the uterus is not entered at operation.
On the other hand, he states that this possibility cannot be denied.
He believes that the arguments which he has set forth in his paper

speak for the possibility of the origin of such growths from the coelom-derived peritoneum, as with similar growths elsewhere in the peritoneum.

I have been interested in endometriosis of laparotomy scars for several years, but had not had an opportunity to study a case of my own until September, 1926, when I encountered one following ventrofixation of the uterus after cutting and ligating both tubes.

If tubal sterilization or salpingectomy is ever in any way responsible for the presence of müllerian mucosa in the abdominal scar, we would expect frequently to find endometriosis of the tubal stump and also of adjacent or adherent structures following operations in which the tubes have been removed or cut and the uterus retained. If it is true that the müllerian mucosa in abdominal scars, following salpin-
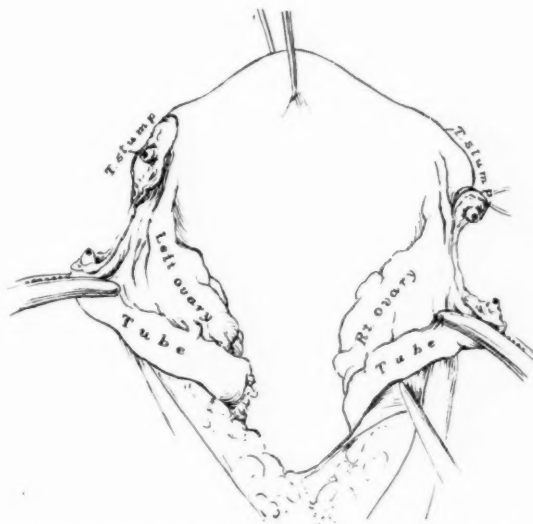

Fig. 1.—Treatment of the tubal stump after salpingectomy (x 2/3.) Some operators excise a part of the interstitial portion of the tube and bury the stump in the uterine cornu. Others remove the tube distal to the uterus and ligate the stump without attempting to bury it. On severing the tube its walls retract, thus exposing the traumatized mucosa. Bits of the latter may be transplanted, during the various proceedures incident to salpingectomy, in the immediate and also in more remote operative fields. The results of the cultivation of tubal mucosa in women, which has been initiated by salpingectomy, may be determined by the histologic study of tubal stumps removed at a subsequent operation.

gectomy, arises from a transformation or differentiation of bits of the peritoneal serosa included in the abdominal wound, as claimed by the supporters of the serosal theory for peritoneal endometriosis, the endometriosis of the tubal stump and neighboring pelvic structures should have a similar origin. If it can be shown that the endometriosis in the latter structures, at times, arises from tubal and uterine mucosa by direct extension and transplantation, a similar origin, at times, might account for the müllerian mucosa in laparotomy scars following salpingectomy.

Since September, 1926, we have been studying the results of salpingectomy and tubal sterilization. Salpingectomy was done on many uteri after their removal. In some the tubal stump was buried in the uterine cornu and in others it was ligated (Fig. 1). In burying the tubal stump care was taken, in some instances, to avoid piercing it with the needle carrying the suture, and in others it was purposely transfixed to determine the result of drawing the bungling doubled catgut suture through the traumatized tube. On severing the tube its muscular walls retract, the mucosa is exposed (Fig. 2) and bits of the latter apparently may be unintentionally transferred by the surgeon to various parts of the field of operation. This chance is increased if the tube is clamped or ligated near its cut end. The transfixing of the tubal stump by a ligature apparently is an efficient way to dis-

Fig. 2.—Photomicrograph (x 10) of a longitudinal section of the stump of a severed tube. Its walls have retracted and its mucosa is exposed like the crayon of a sharpened pencil. The tubal mucosa may be further traumatized by clamping or ligating the stump. In the healing of such a stump the traumatized and exposed mucosa often grow out as sprouts which may invade any organ or structure adherent to the stump.

seminate bits of the tubal mucosa. This experimental material was hardened in formalin and examined histologically in order to ascertain the immediate results of operative trauma on the tube and the possible finding of bits of tubal mucosa in the operative wound. The latter were found in 16 out of 42 tubal stumps studied in this manner (Fig. 3).

I have often observed blood escaping from the abdominal ostia of tubes when the abdominal operation has been preceded by a curettage of the uterus. Bits of the uterine mucosa have been found in the lumen of tubes removed in these operations. After cutting across the uterine end of the tube, blood, at times, may be forced from the cavity of the curetted uterus through the lumen of the cut tube as from

the nozzle of a rubber syringe (Fig. 4). In one instance a bit of tissue was seen to "pop" out of the lumen of the tube. This was picked up on the point of a knife, hardened and sectioned and proved to be a bit of uterine mucosa. Melted gelatine containing barium sulphate was injected through the cervix into the cavities of uteri removed by operation before experimentally removing the tube. It was found that this injection mass often escaped from the severed uterine end of the tube, just as blood escapes through the severed tube when the abdominal operation has been preceded by a curettage. Uteri removed by operation were curetted and the cavity filled with water, cervix clamped and then salpingectomy done. Observations at operation and by experiment demonstrate that in salpingectomy the tube is traumatized and, at times, bits of the tubal and uterine mucosa are transferred by the surgeon to various parts of the field of operation, such
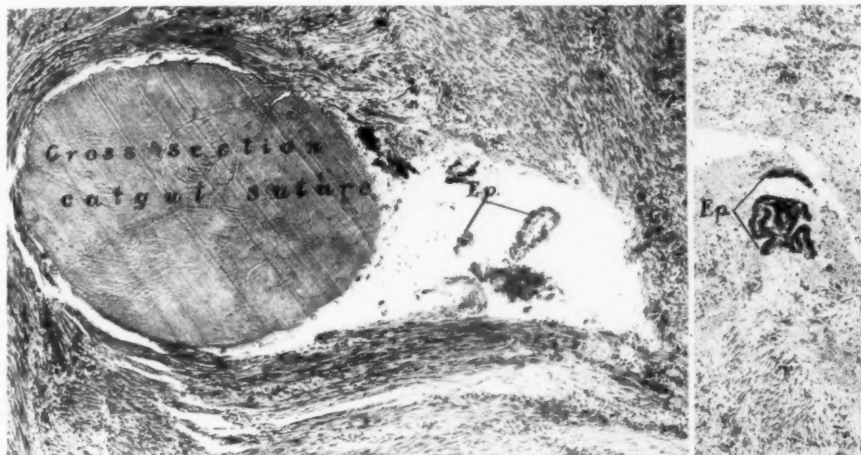

Fig. 3.—Two photomicrographs (x 60) showing "tubal epithelium" transplanted in the uterine cornu during salpingectomy and the burial of the stump. The immediate results of salpingectomy were studied by performing that operation on uteri which had been removed. Fragments of tubal mucosa were found in 16 of 42 specimens, so studied. If tubal epithelium thus transplanted should live, we would expect to find seedlings in and about the tubal stumps removed at the second operation. These seedlings were found.

as the tubal stump, the uterine cornu, the pelvic structures about it and even the abdominal wound. In performing the "toilet" of the peritoneum and in the closure of the abdominal incision after salpingectomy, the surgeon may unknowingly cover the transplanted bits of tubal mucosa, as carefully as in the experimental work of Jacobson[8] and others in their successful autotransplantation of müllerian mucosa in lower animals. What are the results of these unintentional experiments in the cultivation of müllerian mucosa in women? A knowledge of the nature of the original operation and the histologic study of the tubal stumps and the surrounding structures obtained at the second operation enable us to determine these results.

The method of studying these cases was as follows:

1. If hysterectomy was indicated at the second operation, great care was exercised to remove any tissue adherent to the uterine cornu or tubal stump together with the uterus. If hysterectomy was not indicated, the same care was employed in excising the uterine cornu containing the tubal stump.

2. The uterus or specimen to be studied was hardened in formalin. If the specimen promised to be of unusual interest, sketches were made of it before cutting the blocks for histologic study.

3. The blocks were embedded in celloidin and the permanent sections were stained in hematoxylin and eosin.

4. The entire course of the lumen of the tube in the stump was followed and its relation to any misplaced müllerian mucosa was determined. By carefully watching the surface of the block, as the sections are cut, one could usually see

Fig. 4.—If an abdominal operation has been preceded by a curettage of the uterus, blood frequently may be seen escaping from the abdominal ostia of the tubes. If salpingectomy or tubal sterilization is done, blood, at times, may be forced from the cavity of the curetted uterus through the lumen of the tubal stump as through the nozzle of a rubber syringe. Bits of uterine mucosa have been demonstrated in this blood. This represents one way by which uterine mucosa may be transplanted during these operations.

the tube, follow its course, detect an endometriosis, if present, and determine its relation to the mucosa of the tube. The effect was that of watching a slowly moving motion picture. The first complete section was stained, floated on a slide and examined with a hand lens or under the low power of the microscope. If ''uninteresting,'' more sections were cut until the surface of the block indicated a change. Other sections were then stained and examined. If any question arose as to the exact relation between the misplaced müllerian mucosa and that of the tubal stump, complete serial sections were saved and stained until this point was determined. In all cases the entire block or the portion of it showing ectopic müllerian mucosa was cut and all sections were saved until the specimen had been studied. In addition, sections taken at intervals which showed the important features of the specimen were mounted, numbered according to their sequence and

kept. This feature of the work was entrusted to Miss Isabel Peck, who is well trained in laboratory technic and in the histologic diagnosis of müllerian tissue. Without her interest and cooperation this study would not have been accomplished.

THE RESULTS OF THE CULTIVATION OF MÜLLERIAN MUCOSA IN WOMEN AS SHOWN BY THE HISTOLOGIC STUDY OF TUBAL STUMPS FOLLOWING SALPINGECTOMY AND TUBAL STERILIZATION

We have already shown the immediate results of salpingectomy and tubal sterilization. On severing the tube its walls retract and its mucosa protrudes. The tubal mucosa may also be traumatized by clamping, ligating the tube and transfixing it by a ligature. Bits of tubal mucosa, at times, are transplanted in and about the tubal stump and even in more remote portions of the field of operation. The study of
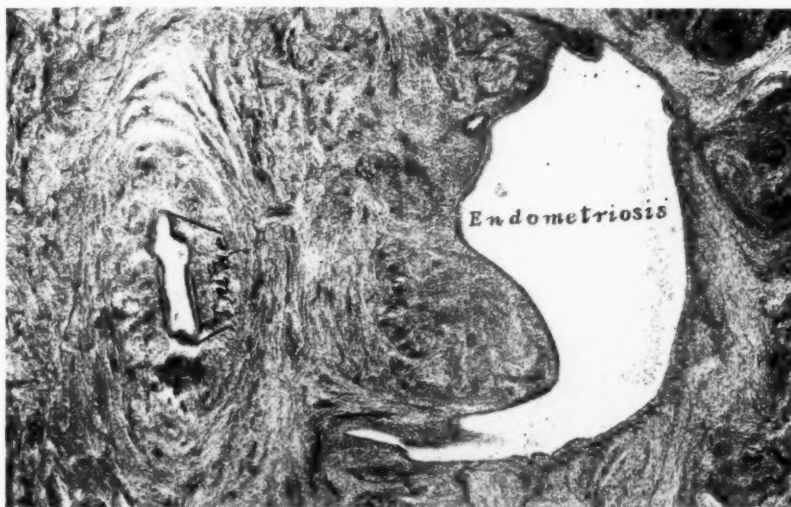

Fig. 5.—Photomicrograph (x 25) of a portion of the uterine cornu, containing a tubal stump, tube and ovary removed nineteen years before the last operation. A wedge-shaped piece of the uterine cornu was described as having been removed with the tube at the first operation. The tube is shown in cross-section (very close to the end of the stump) with an endometriosis lateral to it. It was definitely determined that this misplaced "endometrial" tissue did not arise from the tubal mucosa by direct extension or sprouts. Circumstantial evidence indicates that it is a seedling, possible from bits of tubal mucosa transplanted at the first operation.

tubal stumps and adjacent or adherent structures, removed at a subsequent operation, should show the results of the unintentional cultivation of tubal mucosa initiated at the first operation.

Since September, 1926, we have been collecting and studying tubal stumps. A few were obtained from specimens removed prior to that date. Two were from autopsies (courtesy of Dr. V. C. Jacobson) and the remaining were removed since September, 1926. Tubal stumps, often with structures adherent to them, were obtained from 36 patients. As bilateral salpingectomy or tubal sterilization had been done in 15 of these patients, 51 tubal stumps were available for histologic study.

An attempt was made to ascertain the occasion of the original operation, but in many instances this was only partially successful. In the majority of the cases one tube and ovary or both tubes and one ovary were reported to have been removed for salpingitis or its results. In 6 cases a ventrofixation of the uterus preceded by tubal sterilization had been done. In 2 of these one tube and ovary had been removed. In 2 other patients an "ovarian cyst" had been removed. In 3 patients the first operation had apparently been for an endometrial hematoma of the ovary and its associated peritoneal endometriosis, though not so recognized by the operator. There was only 1 instance of tubal pregnancy in the series of original operations. The majority of the
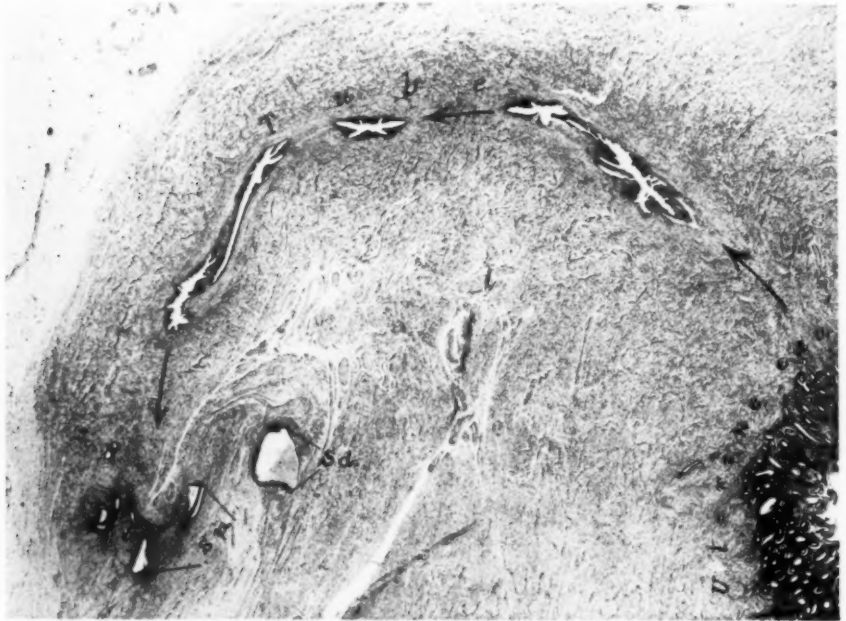

Fig. 6.—Photomicrograph (x 10) of a longitudinal section, in a perpendicular plane, of the right uterine cornu, tube and ovary removed eleven years before for a fibroma of the ovary. Tubal sterilization was done on the opposite side and the uterus fixed to the abdominal wall. The tube was severed close to the uterus and its stump buried. The course of the interstitial portion of the tube is well shown and its lumen was followed (in other sections) to the end of the stump where sprouts (*sp*) of the tubal mucosa have invaded the tissues about the stump. A seedling (*sd*) is present mesial to the sprouts. It is of the same histologic structure as the latter, but was shown not to be continuous with them. Circumstantial evidence indicates that it might have grown from tubal epithelium transplanted at the first operation.

second operations were undertaken for the relief of pain caused by "adhesions." In 8 of these endometriosis apparently was the principal cause of the adhesions and discomfort, in 3 of which a peritoneal endometriosis was probably present at the first operation. Four patients were operated upon for uterine leiomyomata, 3 for tubal pregnancy, 3 for uncontrollable uterine bleeding and 1 for cancer of the uterine cervix.

An endometriosis was found in or about the tubal stumps in 30 of the 36 patients. As bilateral salpingectomy or tubal sterilization had been done in 15 instances, 51 stumps were studied. Endometriosis was found in 42 of these. Where 2 stumps were obtained from one patient, if endometriosis was found in one, it was also present in the other and furthermore there was a great similarity in the type of lesion in both stumps. The endometriosis usually resulted from sprouts growing out from the mucosa of the tubal stump (Figs. 6, 7, 8, and 9) but occasionally arose as seedlings springing up in situations where we know that bits of tubal mucosa might have been transplanted at the first operation. The evidence that many of these seed-
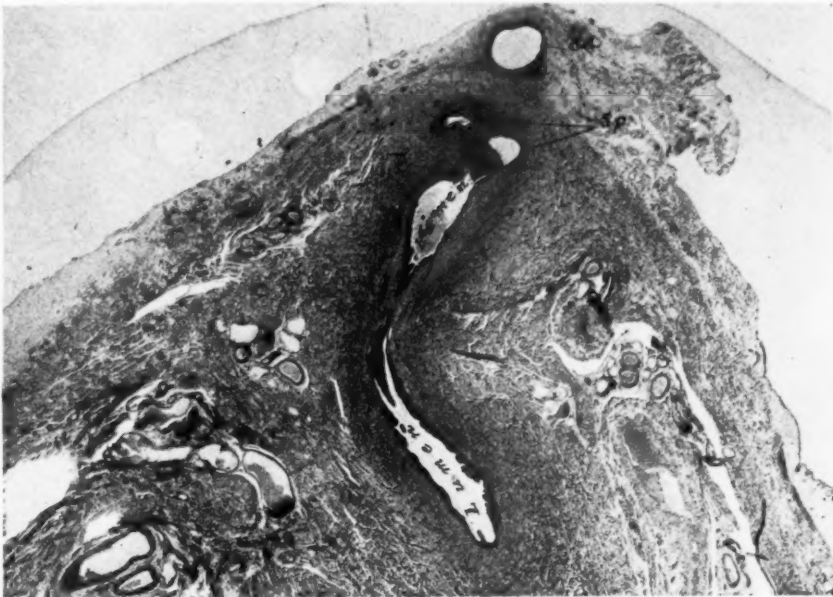

Fig. 7.—Photomicrograph (x 10) of a longitudinal section, in a horizontal plane, of the left uterine cornu, the seat of a previous sterilization (same case as the preceding). The interstitial portion of the tube is well shown with sprouts (*sp*) of the tubal mucosa in the uterine wall about the end of the stump and distal to these is a seedling (*sd*) with the same histologic structure as the sprouts but not continuous with the latter. If tubal epithelium transplanted a few millimeters from the end of the stump grows, it might grow if transplanted at a greater distance, and it also might grow if transplanted during other operations than salpingectomy and by other means than operations.

lings arose from this source was most convincing to me, but at best this evidence is only circumstantial. Positive proof of such an origin cannot be furnished. It may be claimed that the seedlings were present at the first operation or came from a differentiation of peritoneal mesothelium included in the operative wound or were originally sprouts, portions of which became "pinched off" by the reaction of the surrounding tissue. On the other hand, the evidence that the sprouts arose from pre-existing tubal mucosa and *not* from peritoneal

mesothelium was positive. The histologic structure of the seedlings and the sprouts was the same.

Seedlings without any evidence of sprouts were found in specimens from only three patients. Both seedlings and sprouts were found in specimens from four patients. I believe that this number should be much greater, as it is often very difficult and even impossible to exclude the presence of seedlings in specimens with an extensive endometriosis.
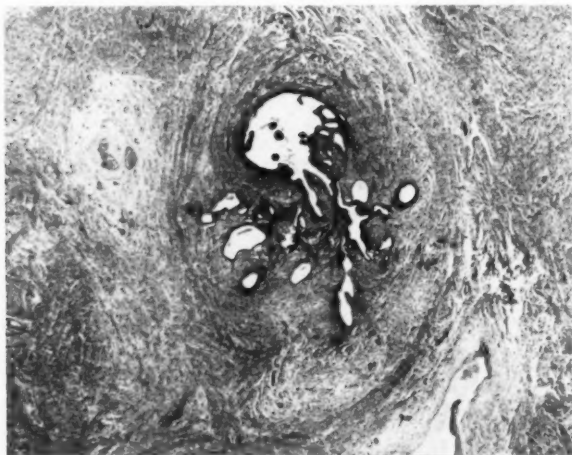

Fig. 8.—Photomicrograph (x 10) of a cross-section of a tubal stump at its distal end. The traumatized mucosa has become activated and has partially filled the lumen of the tube and as sprouts has invaded the tissues of the uterine cornu in which the stump had been buried at the first operation a year before. The distal extensions of the sprouts are shown in the next illustration.
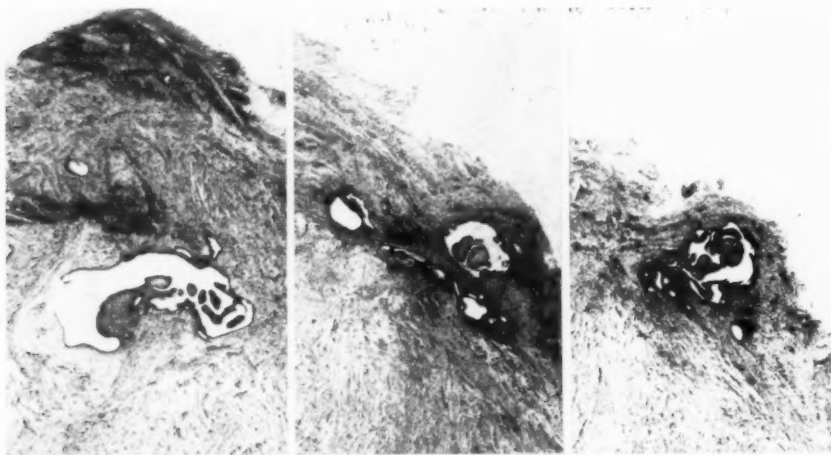

Fig. 9.—Three photomicrographs (x 10) from a series of cross-sections showing the distal extension of the endometriosis originating from the traumatized tubal mucosa of Fig. 8. It has extended almost to the peritoneal surface of the uterine cornu. Histologically it is of tubal type and resembles many of the lesions in peritoneal endometriosis of possible implantation origin.

Sprouts without demonstrable seedlings were present in and about the tubal stumps obtained from 23 patients.

Many interesting questions arise. Why does endometriosis not occur in all cases? Will it develop in women operated upon after the menopause? Will it occur if all ovarian tissue is removed at the first operation? Why is it insignificant in some and extensive in others?

In all cases the first operation was done before the menopause. In only two of the patients had both ovaries been removed. In the tubal stumps (four in number) from those two cases, no evidence of endometriosis was found. Endometriosis developed both in the patients operated upon for salpingitis and for tubal sterilization and apparently to the same degree. The condition present at the first operation apparently did not determine whether or not an endometriosis arose or its extent. The method of salpingectomy also seemed to have no influence

Fig. 10.—Three photomicrographs (x 10) from a series of cross-sections of a tubal stump which had been buried in the uterine cornu. The distal end of the stump appears in the third photomicrograph. Here histologically typical uterine mucosa, apparently arising from the traumatized and activated mucosa of the stump, has grown back, as a polyp, into the dilated lumen of the interstitial portion of the tube (see first two photomicrographs). This mucosa has invaded the uterine cornu beyond the stump. For a further extension of this invasion, see the next illustration. The dilated gland (sd) probably is a seedling. At a previous operation, two years before, the uterus was curetted, the pelvic floor repaired, both tubes and one ovary removed for salpingitis, and the uterus fixed to the abdominal wall. On severing the uterine end of the tubes, blood escaped from the uterine cavity through the lumen of the tubal stumps. Did the endometrial tissue in the distal end of the stump arise from the transplantation of a bit of uterine mucosa at the former operation or from a differentiation of the traumatized tubal mucosa? From a study of this and other specimens, I believe the latter.

upon the incidence or the extent of the endometriosis. It occurred both in patients in whom the tube had been removed and the stump ligated distal to the uterus and also in those in whom the tubal stump was buried in the uterine cornu.

When both tubes had been removed or incised and one or both ovaries retained, there was a great similarity in the endometriosis of both tubal stumps. This suggests that the tubal mucosa and its inherent ability to become invasive are usually the same in both tubes

of the same person, though often differing among individuals. This manifestation of a difference may not be peculiar to the individual, but may be due to other factors, possibly to the phase of the menstrual cycle in which the operation occurred.

In some instances the endometriosis was of tubal and in others of uterine type. The differentiation of tubal into uterine mucosa was one of the most interesting features of these lesions (Figs. 10, 11, 12, 13, and 14). We were unable to ascertain the factors which influenced its development. It followed salpingectomy for salpingitis and also for noninfected tubes. It occurred after tubal sterilization as well as salpingectomy and also in cases in which the tube had been removed distal to the uterus and its stump ligated as well as in salpingectomy with burial of the tubal stump in the uterine cornu. The
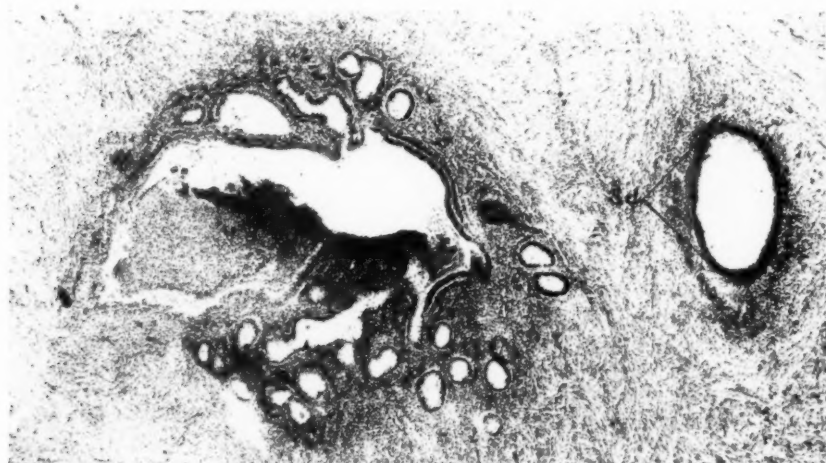

Fig. 11.—Photomicrograph (x 25) of a section of the uterine cornu from the series shown in the preceding illustration and distal to these. An endometrial cavity, arising from the direct extension of the endometrial tissue shown in Fig. 10 and partially filled with blood, is present. The blood evidently came from the mucosa lining this cavity as indicated by hemorrhage in its stroma. The patient was bleeding at the time of the operation. The mucosa of this ectopic endometrial cavity possibly was influenced to bleed by the same impulse as was the mucosa of the uterine cavity. The seedling (sd), shown in the preceding photomicrograph, also appears in this one.

possibility of the transplantation of uterine mucosa escaping from a preliminary curettage was considered in a few of the cases, but some of the patients had had no preliminary curettage. In the majority of cases the endometriosis, resulting from salpingectomy, was slight and only of scientific interest. In others, however, it was extensive and was responsible for the second operation. An endosalpingiosis or so-called adenomyoma evidently was present in the tubes at the first operation in two patients and might have been present in others. The second operation in each of these cases was for tubal pregnancy. Endometriosis (endosalpingiosis) was found in the interstitial portion of the tube on the side of the tubal pregnancy and also in the tubal
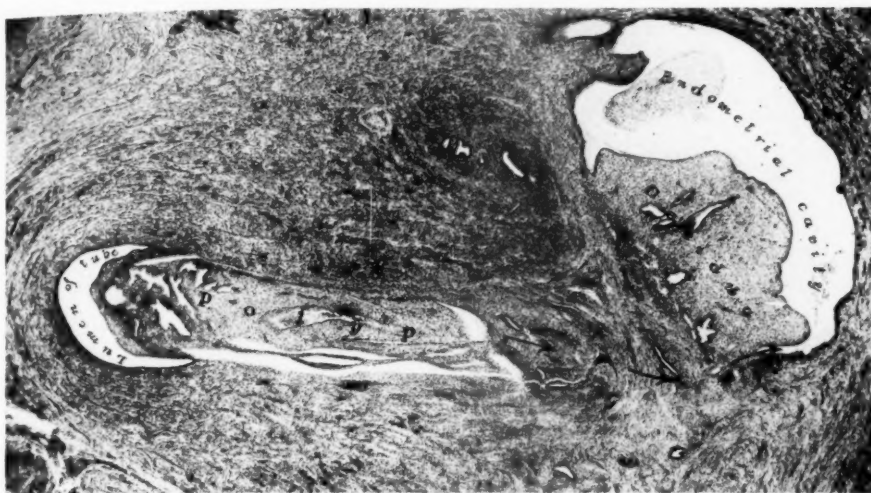
Fig. 12.—Photomicrograph (x 10) of a longitudinal section, in a horizontal plane, of a uterine cornu with a buried tubal stump. It shows the same sprouting of the traumatized mucosa of the distal end of the stump as that indicated in Figs. 10 and 11. Like the latter it has grown back into the lumen of the stump as a polyp and has invaded (see arrows) the uterine cornu distal to the stump forming ectopic endometrial cavities lined by uterine mucosa with a definite decidual reaction. The first operation, ten years before, had been a ventrofixation with an attempted tubal sterilization. An ectopic pregnancy was present in the opposite uterine cornu, possibly situated in one of the ectopic endometrial cavities resulting from the extension of the traumatized tubal mucosa. A decidual reaction was found in the mucosa of the uterine cavity, in that of the ectopic endometrial cavities of both uterine cornua but not in the mucosa of the tubes proper.

Fig. 13.—Photomicrograph (x 10) of a longitudinal section, in a perpendicular plane, of a tubal stump ligated distal to the uterine cornu in a right salpingo-oöphorectomy four years before. It would seem that the tube had been ligated at x. The dilated lumen of the interstitial portion of the tube is well shown. An endometriosis of the tubal stump is present back of and also distal to the apparent site of ligation. Both may have been initiated by the trauma of the ligature, or tubal endometriosis might have been present at the time of the first operation. Clamping the tubal stump at the first operation also might have contributed to the endometriosis of this section.

stump of the opposite side (tube removed at previous operation) in each case. In both situations the histologic structures of the two lesions were similar.

Trauma, other than operative, may be a factor in the etiology of tubal endometriosis as indicated by an endometriosis of the tubal stump found in a patient with spontaneous amputation of the right tube and ovary.

ENDOMETRIOSIS OF THE OVARY FOLLOWING SALPINGECTOMY

In 1926 Dougal[9] described a case of endometriosis of the ovary after removal of both tubes and the opposite ovary for gonorrheal salpingo-

Fig. 14.—Anterior view (x 2/3) of the uterus, both tubal stumps, and the left ovary, Case 1. The right tubal stump, ligated distal to the uterus, is adherent to the indurated mesosalpinx and broad ligament (Fig. 15). The left tubal stump is adherent to the mesial surface of the ovary. The latter contains an endometrial cyst or hematoma. See Figs. 16 and 17.

oöphoritis eleven and a half years before. A typical adenomyoma was present in both uterine cornua and the ovary was adherent to the posterior surface of the uterus near the left cornu. He offered three possible explanations for the origin of the endometrial tissue in the ovary after the removal of both fallopian tubes:

1. The endometrial tissue may have been in the ovary before the tubes were removed.

2. One or either stump of the tubes may have been left patent after the operation, and so allowed fragments of endometrium to escape into the peritoneum during menstruation.

3. The endometrium may extend directly from the uterine cavity to the ovary through intervening structures by infiltration.

He believes that the latter is the correct one in his case for the following reasons: An adenomyoma in both uterine cornua strongly suggests that the uterus was primarily responsible for the growth in the ovary. The presence of islands of endometrium, dotted about through the tissues intervening between the uterine cavity and the
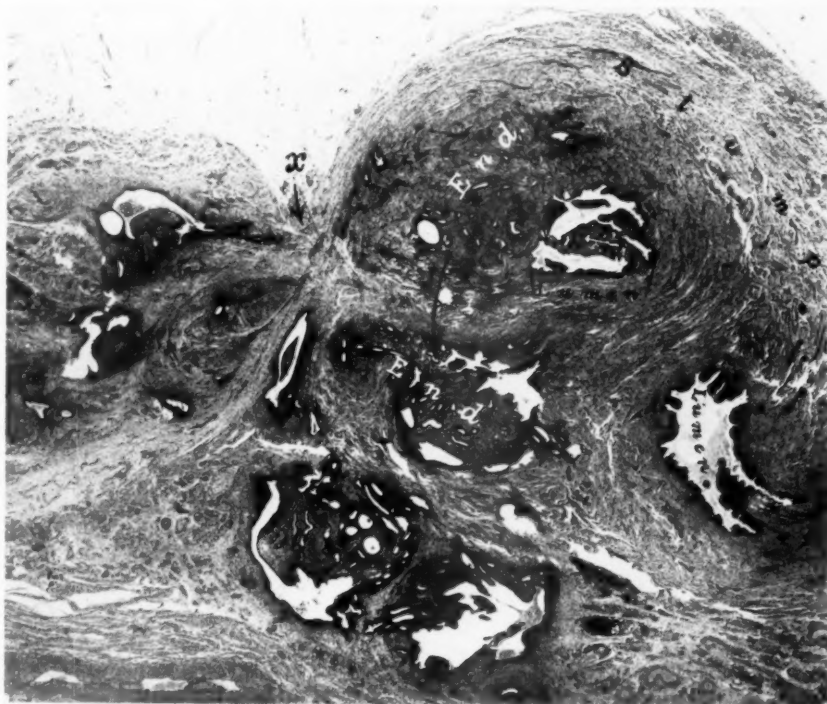

Fig. 15.—Photomicrograph (x 10) of a longitudinal section of the right tubal stump of Fig. 14. The stump apparently had been ligated distal to the uterine cornu at x. The lumen of the tube was traced (in other sections) almost to the end of the stump, where it is partially restored by the repair following the trauma of the ligature. An endometriosis "End" evidently arising from the traumatized tubal mucosa, back of the ligature, has invaded not only the end of the stump but also the tissues of the mesosalpinx and broad ligament beneath it. The endometriosis of the structures beneath the stump and directly continuous with that of the latter has become activated to form typical uterine mucosa without any evidence of a reaction to menstruation. Endometriosis, such as this, might invade any organ or structure adherent to the stump.

adherent ovarian cyst would appear to indicate that the extension had been by infiltration from the mucosa of the uterine cavity to the ovary.

I have encountered 4 cases of endometriosis of the ovary in patients who had had a previous salpingectomy.

CASE 1.—Endometriosis of the left ovary and of both tubal stumps after left salpingectomy and right salpingo-oöphorectomy. Patient, aged thirty-four, had one child, aged thirteen and a miscarriage two years later. The appendix was removed in the year 1909 and in 1919 both tubes, the right ovary and part of the left ovary were removed for bilateral salpingitis. The uterus was suspended. The tubes were described as being closed at the last operation and no evidence of ovarian hematomas or endometrial tissue in the pelvis was observed.

The present complaint was severe menstrual pain and also pain independent of menstruation. Pelvic examination showed the uterus to be in normal position, its movements restricted and a nodular induration in the culdesac. A preoperative diagnosis of endometriosis was made. The third operation at the Albany Hospital, May 2, 1927, showed the uterus to be in normal position. The stump of the right tube was fused with the indurated tissues of the broad ligament beneath it. The stump of the left tube was adherent to the mesial surface of the ovary. A slight amount of endometriosis was present in the posterior culdesac. The uterus with the portion of the broad ligament adherent to the right tubal stump was
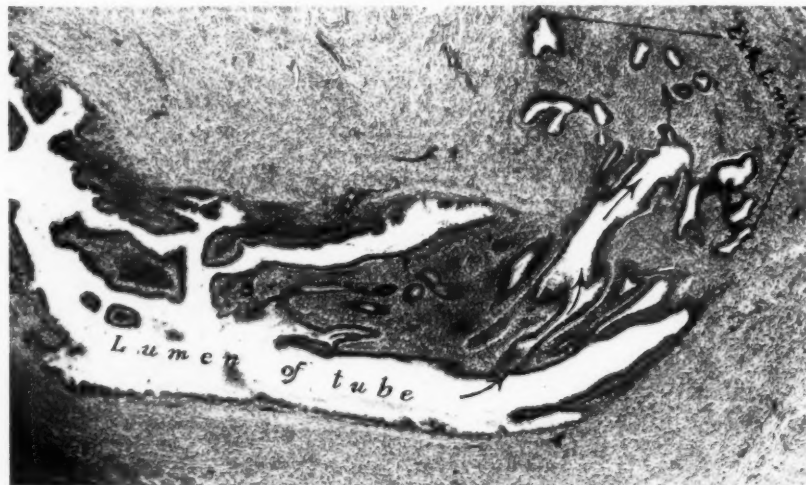

Fig. 16.—Photomicrograph (x 25) of a portion of a cross-section of the left tubal stump (Fig. 14). The lumen of the distal end of the stump is shown. The mucosa has become activated partially filling the lumen of the tube and also invading the wall of the stump, thus forming an endometriosis in this situation. For a further extension of this endometriosis, see the next illustration.

carefully removed, together with the left ovary (Fig. 14). In freeing the latter the walls of an ovarian hematoma were torn, as usually occurs in removing adherent endometrial hematomas of the ovary.

An endometriosis was present in the right tubal stump evidently arising from the growth of tubal mucosa injured by ligating the stump (Fig. 15). This had extended through the wall of the stump and had invaded the underlying tissues of the broad ligament. A similar sprouting of the mucosa of the left tubal stump was found (Fig. 16) which had invaded the structures adherent to it, including the left ovary. It was also demonstrated that the müllerian mucosa, lining the portion of the hematoma of the left ovary adherent to the tubal stump, was directly continuous with the mucosa of the tube through the invasion just described (Fig. 17).

It is impossible to state whether the endometriosis in the culdesac arose from the previous operation or was present at that time. It may be claimed that

endometrial tissue was present in the ovaries at the first operation and endometriosis of the tubal stumps arose from this. However, the indications that the müllerian mucosa in the left ovary arose from the direct extension of the traumatized mucosa of the tubal stump are as follows:

1. It was shown to be continuous with it (Fig. 17).

2. The müllerian mucosa in the ovary had invaded that organ from its mesial surface, the surface adherent to the tubal stump. Endometrial tissue in the ovaries of patients who have not had a previous operation nearly always occurs on the lateral and under surfaces of that organ.

3. A similar endometriosis was present in the opposite tubal stump (ovary removed) with invasion of the adherent structures (Fig. 15).
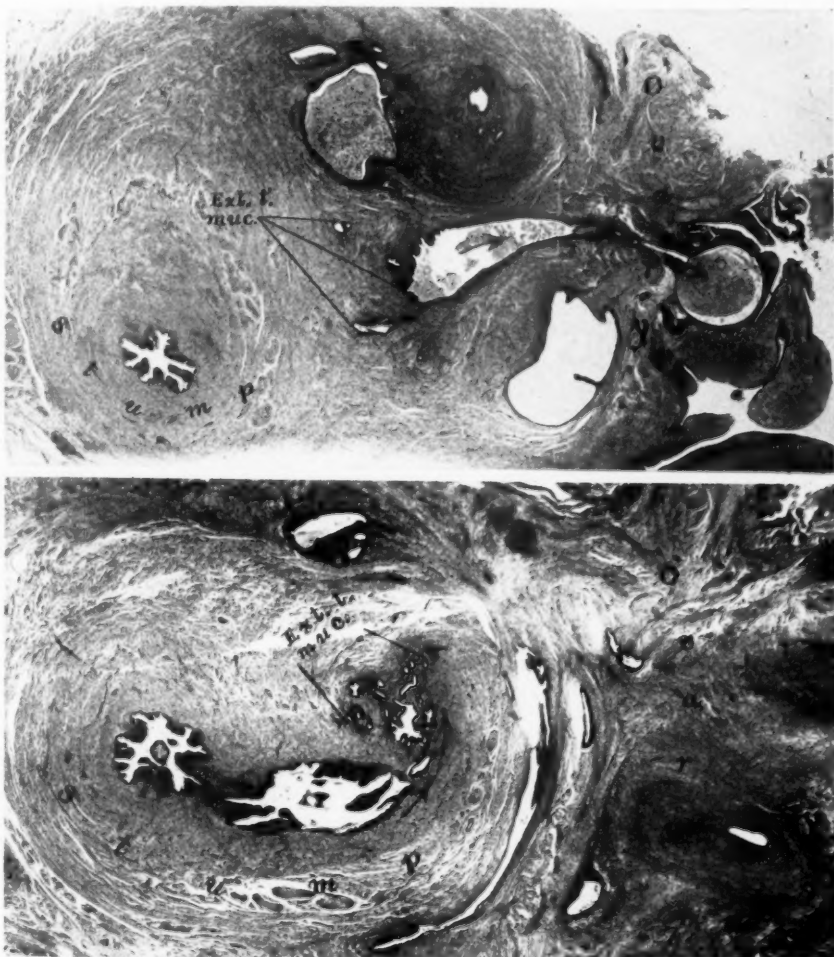
Fig. 17.—Two photomicrographs (x 10) of cross-sections of the left tubal stump and portions of the ovary adherent to it. The lower photomicrograph shows a continuation of the endometriosis (Ext. t. muc.) which arose from the direct invasion of the stump by its mucosa. (See Fig. 16.)

The upper photomicrograph demonstrates a further extension of this endometriosis and that the latter is continuous with the endometrial lining of the portion of the ovarian cyst adherent to the stump. This indicates that the endometrial lining of the cyst might have arisen from the direct extension of the traumatized mucosa of the tubal stump into the adherent ovary (ovary had been resected).
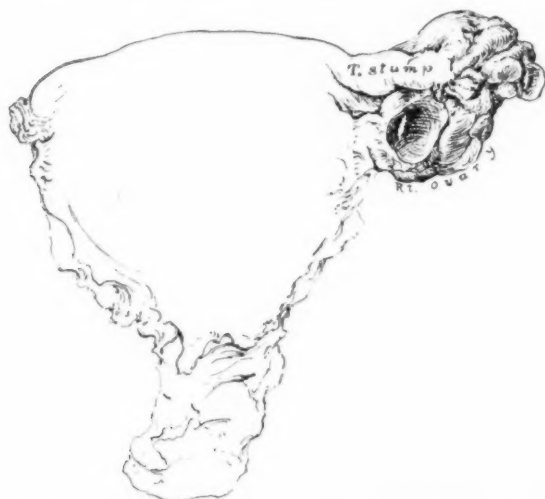
Fig. 18.—Posterior view (x 2/3) of the uterus and right tubal stump and ovary, (Case 2). The stump of the right tube is adherent to the mesial surface of the right ovary. See the next illustration.
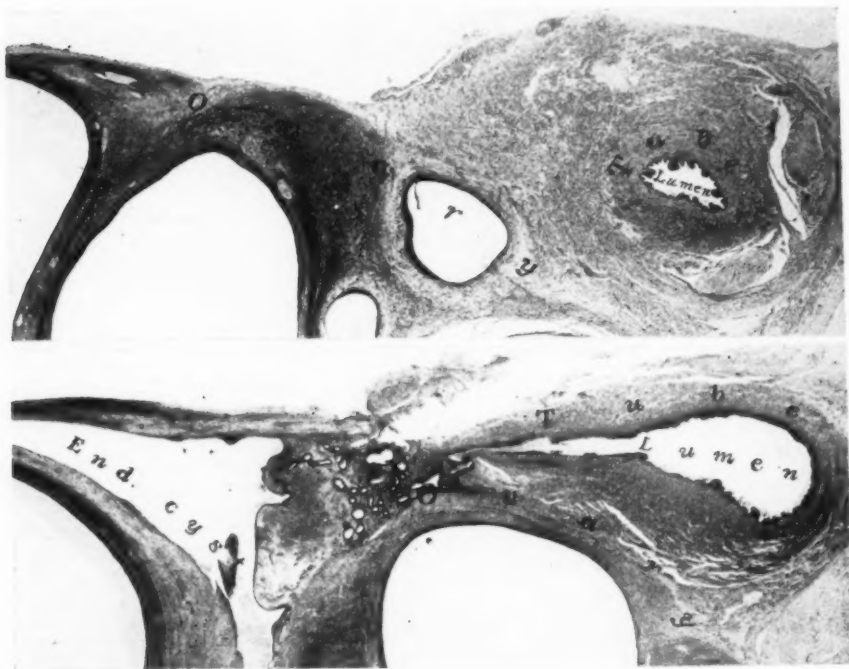
Fig. 19.—Two photomicrographs (x 10) from a series of sections demonstrating the relation of the tube to the ovary of Fig. 18.

The upper photomicrograph, of a cross-section of the stump near its base, shows a normal appearing tube adherent to the ovary. As these sections were followed toward the tip of the stump, a small endometrial cyst of the ovary appeared lateral to the stump.

The lower photomicrograph shows the origin of the endometrial lining of the cyst from tubal mucosa by direct extention through the wall of the tube traumatized at the first operation.

CASE 2.—Endometriosis of the right ovary, directly continuous with the mucosa of the tubal stump, following right salpingectomy. Patient, aged thirty-four, married twice but never pregnant, complained of severe pain in the right lower abdomen. Menstruation was painless. The patient had had a conservative operation in 1924 for bilateral salpingitis, being very anxious to have children. The operative procedures at the first were as follows: appendicectomy, resection of half of the right ovary, right salpingectomy and removal of the distal end of the left tube. At the second operation, May 12, 1927 at the Albany Hospital, the uterus was found to be retroflexed and adherent; the stump of the right tube was adherent to the mesial surface of the right ovary; the left ovary appeared normal and the shortened left tube was occluded, but free from adhesions. The uterus, right tube, and ovary were removed (Fig. 18).

The histologic study of the right ovary with adherent tubal stump showed a small endometrial hematoma of the ovary, the mucosa of which was continuous with
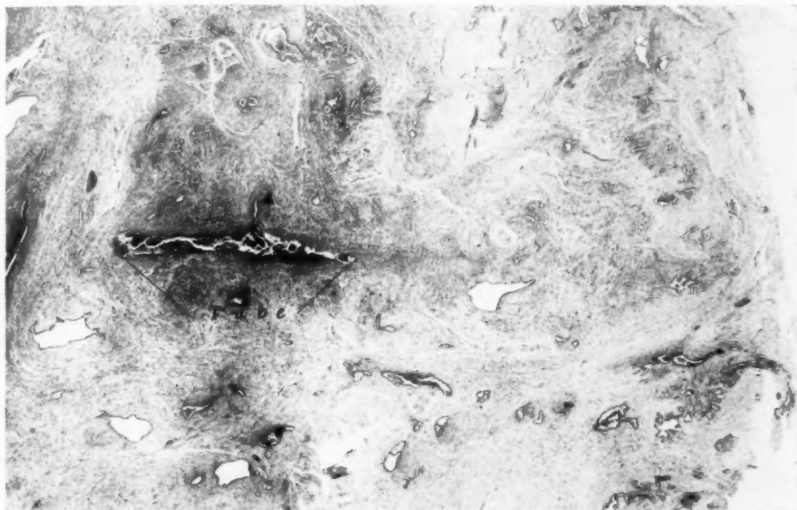
Fig. 20.—Photomicrograph (x 8) of a longitudinal section of the right uterine cornu (Case 3). Right tube and ovary and left tube had been removed. The specimen was obtained, at autopsy, from a patient dying of diphtheria. An endometriosis is present, evidently arising from the direct extension of the tubal mucosa.

the mucosa of the tubal stump by direct extension (Fig. 19). The indications that the endometrial tissue in the ovary was derived from the mucosa of the tube are as follows:

1. It was shown to be continuous with it.

2. It was present near the mesial and not the lateral or under surface of the ovary as occurs in endometriosis of the ovary of nonoperative origin.

3. It was the only endometriosis found in the specimen.

CASE 3.—Endometriosis of the left ovary and both tubal stumps following left salpingectomy and right salpingo-oöphorectomy. The patient, aged thirty-two, was admitted to the contagious department of the Albany Hospital in a dying condition from diphtheria. She lived only a few hours. A postmortem examination was obtained and through the courtesy of Dr. V. C. Jacobson, I had an opportunity to study the pelvic organs. The right tube and ovary and the left tube had been removed. The date of the operation was not obtained. An endometriosis was

present in the right uterine cornu and surrounding tissue from a direct infiltration by the mucosa of the interstitial portion of the tube (Fig. 20). A similar condition was also present in the left uterine cornu. In addition the mucosa of the tubal stump, distal to the uterine cornu, had invaded the tissues adherent to it including the left ovary (Fig. 21). Three small endometrial hematomas were present in the left ovary. The müllerian lining of these was found to be continuous with the "streams" of tubal mucosa arising from the mucosa of the tubal stump and invading the structures adherent to it (Fig. 22). The indications that the endometrial tissue in the ovary (Fig. 23) was derived from the mucosa of the tube are as follows:

1. Three small endometrial hematomas were present in the ovary and all were shown to be continuous with tubal mucosa which had escaped from the tubal stump by direct extension.

2. The hematomas were of the same size and, therefore, apparently of the same age.

3. These hematomas were situated near the mesial surface of the ovary.
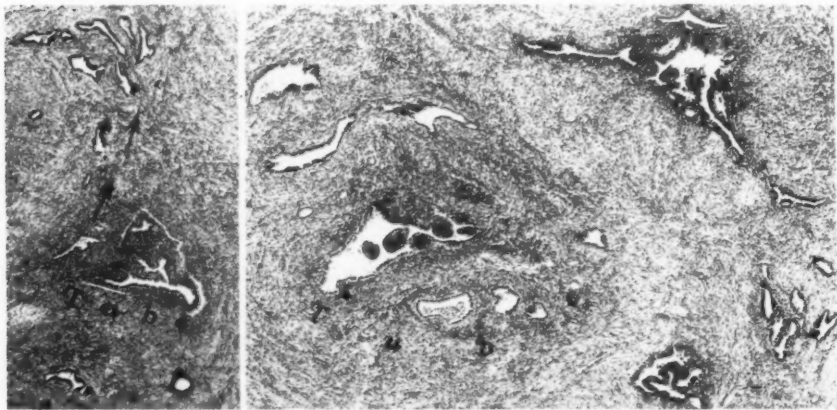
Fig. 21.—Two photomicrographs (x 25) from a series of cross-sections of the left tubal stump and adherent tissues distal to the uterine cornu, possibly where the stump had been ligated. The tube apparently has been traumatized (theory) and its mucosa has grown out from the tube and invaded the surrounding structures.

4. An endometriosis was also present in the tissues about the opposite tubal stump, the ovary having been removed.

5. Endometriosis was found only about the tubal stumps, including the adherent left ovary.

CASE 4.—Endometriosis of the right ovary and both tubal stumps after right salpingectomy and left salpingo-oöphorectomy. Patient, aged thirty-five, had one child, aged sixteen years and two miscarriages, the last one twelve years ago. Nine years ago the appendix, left tube and ovary, and the right tube had been removed for bilateral pyosalpinx. The present complaints were profuse menstruation, bleeding independent of menstruation, leucorrhea, dysmenorrhea, and a sense of a lack of support. Pelvic examination showed a weakened pelvic floor, hypertrophied cervix with eversion of the cervical mucosa, and the uterus in descensus. The second operation was at the Albany Hospital December 3, 1927. The right ovary was adherent to the tubal stump of that side. The portion of the ovary adherent to the stump was resected and removed with the entire uterus. (Fig. 24). The pelvic floor was repaired. An endometriosis was present in the left tubal stump from the direct extension or sprouting of the mucosa of the

end of the stump. An endometriosis was also present in the tissues of the mesosalpinx distal to the stump and apparently arising as seedlings from transplanted tubal mucosa. Their continuity with the sprouts in the stump was not established (Fig. 25). A similar sprouting of the mucosa of the end of the right tubal stump was present. Small patches of müllerian mucosa of a structure identical with that of the sprouts from the tubal mucosa were present in the stump (Fig. 26), in the adhesions (Fig. 27), between the tubal stump and the ovary, and in the portion of the ovary adherent to the stump. Hematomas were present in some
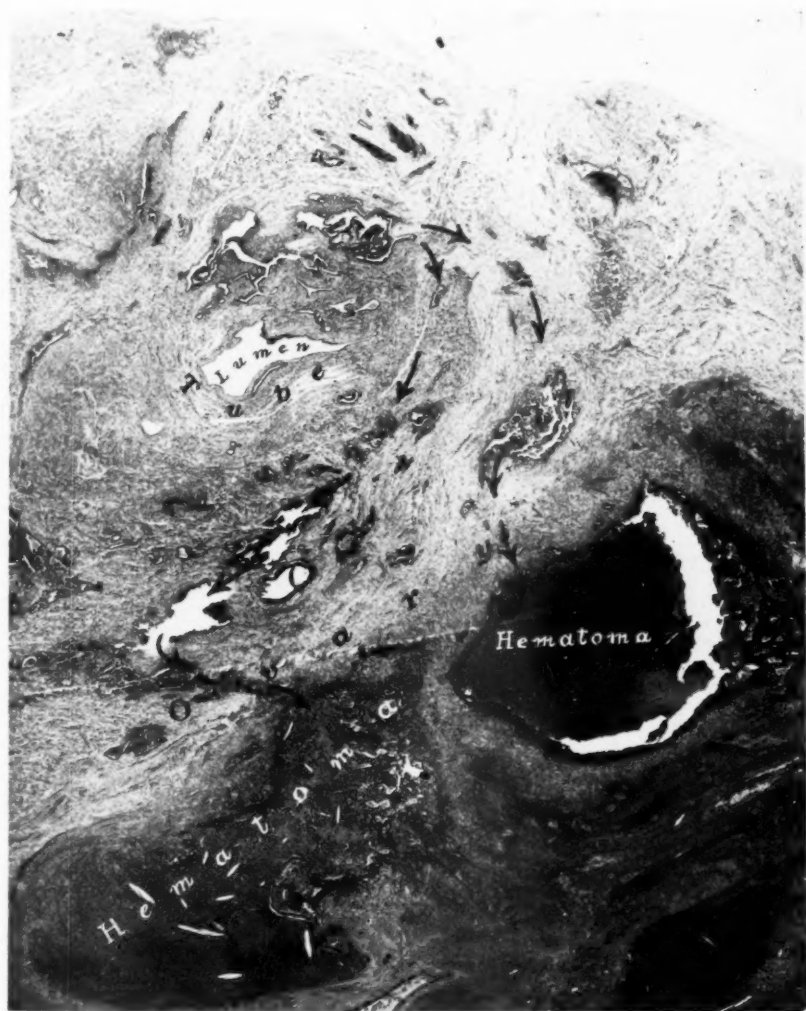
Fig. 22.—Photomicrograph (x 10) of a cross-section of the left tubal stump and adherent structures, including the ovary, distal to the sections shown in the preceding illustration and therefore, distal to the site of apparent ligation of the stump (from the same series of sections as the preceding). The dilated lumen of the stump is well shown with an endometriosis in its walls and streams of tubal mucosa invading the surrounding structures. The preceding illustrations indicated that these streams of mucosa arose from the mucosa of the tubal stump. Two endometrial hematomas or cysts are shown in the adherent ovary. The streams of tubal mucosa, just described, were found to empty into these hematomas. See arrows.

of these foci in the ovary. These patches of müllerian-like tissue, just described, appeared to be seedlings and were not continuous with the sprouts from the mucosa of the stump. The indications that the ''müllerian'' mucosa in the ovary arose from tubal epithelium transplanted at the first operation are as follows:

1. The study of the immediate results of salpingectomy show that tubal epithelium, at times, is transplanted by the surgeon.

2. The seedlings in this case were found where such "seeds" might easily have been sown.

3. They were present in the tubal stump itself, in the adhesions between it and the ovary and in the portion of the ovary adherent to the stump.

4. The histologic structure was identical with that of the sprouts arising from the tubal mucosa.

5. They were not continuous with the mucosal sprouts.

6. They were present on the mesial surface of the ovary.

7. Similar seedlings were found in the tissues about the opposite tubal stump, on which side the ovary had been removed.
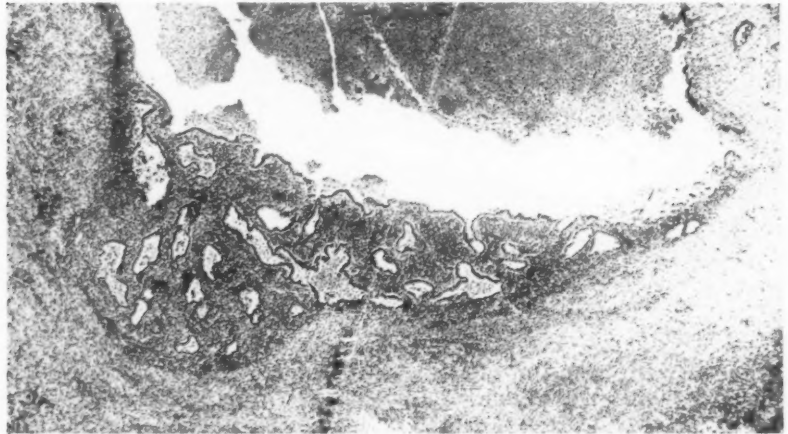
Fig. 23.—Photomicrograph (x 25) of a portion of the endometrial lining of one of the hematomas shown in the preceding illustration. The evidence that these ovarian hematomas arose from tubal mucosa by direct extension is as follows: The mucosa of the tubal stump was shown to have extended beyond the stump, thus invading the surrounding structures. These streams of tubal mucosa could be traced to. i.e., emptied into the ovarian hematomas. The hematomas are nearly of the same size and, therefore, possibly of the same age. They are situated near the mesial and not the lateral or under surfaces of the ovary where endometrial hematomas of nonoperative origin usually arise. A similar endometriosis of tubal origin was present about the opposite tubal stump on which side both the tube and the ovary had been removed.

ENDOMETRIOSIS OF THE ABDOMINAL SCAR FOLLOWING SALPINGECTOMY AND TUBAL STERILIZATION

Several cases of endometriosis of the abdominal scar after salpingectomy have been reported. Nicholson collected 6 from the literature and 15 following ventrofixation of the uterus. As many operators perform tubal sterilization before fixing the uterus to the abdominal wall, the lumen of the tube might have been incised in some of the reported cases of ventrofixation. It is possible in all cases of salpingectomy and tubal sterilization that müllerian epithelium may be

transplanted to the abdominal wound.   This has been recognized by
others who have reported cases of endometriosis of laparotomy scars.
Nicholson states that the anatomic continuity between the epithelium
of the uterine mucosa and that of the tumors of the abdominal wall
was not established in a single instance in the cases collected by him.
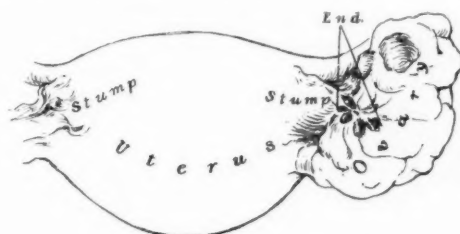
Fig. 24.—Fundus of the uterus and the adherent right ovary (natural size).   The
left tube and ovary and the right tube had been removed nine years before for sal-
pingitis (Case 4).   The ovary is adherent by its mesial surface to the right uterine
cornu with the gross evidence of an endometriosis of the portion of the ovary ad-
herent to the tubal stump.   See also Figs. 25, 26, and 27.
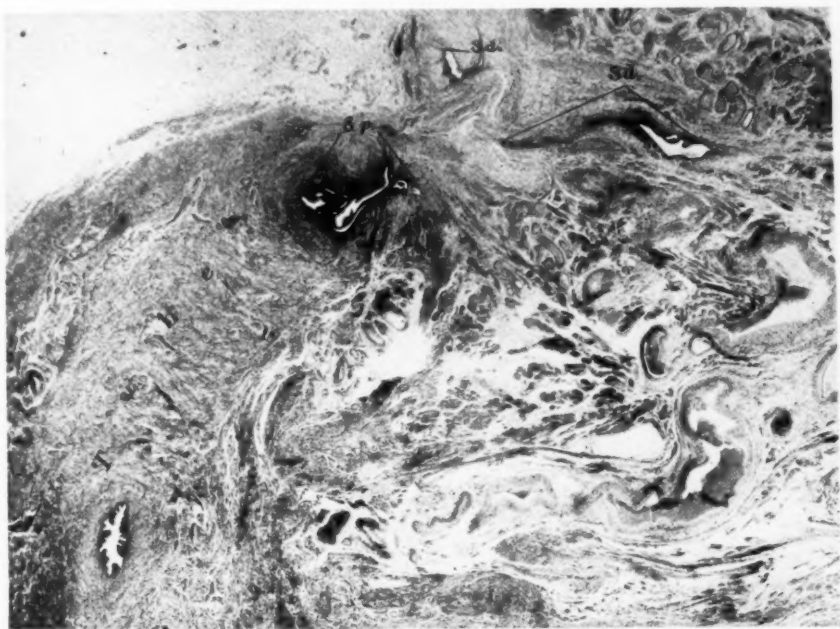
Fig. 25.—Photomicrograph (x 10) of a longitudinal section, in a perpendicular
plane, of the left uterine cornu including the tubal stump.   The stump had apparently
been ligated at *x*.   The walls of the tube can easily be seen and in one place its lu-
men.   The lumen was followed (other sections) to the end of the stump where sprout-
ing (*sp*) is present.   Seedlings (*sd*) are present in the tissues distal to and adherent
to the stump.   These seedlings have the same histologic structure as the sprouts and
are not continuous with them.   The evidence indicates that these seedlings arose from
tubal mucosa "tied off" or otherwise transplanted at the first operation.

I have encountered only 2 instances of endometriosis of the abdom-
inal wall following ventrofixation with tubal sterilization (in one case
one tube and ovary had been removed).

CASE 5.—Endometriosis of both uterine cornua and the left rectus muscle following ventrofixation of the uterus. Patient, aged thirty (three children) had been operated on by me in September, 1921, for prolapse of the uterus. The cervix was amputated, the pelvic floor repaired and after severing and ligating both tubes, the fundus of the uterus was fastened, extraperitoneally, to the ab-
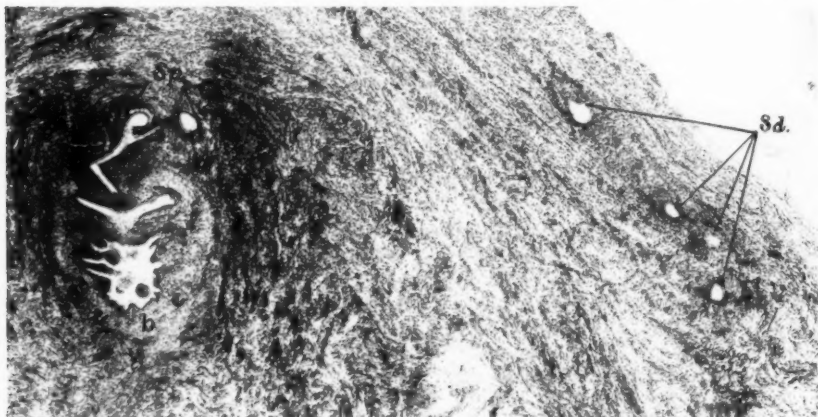
Fig. 26.—Photomicrograph (x 25) of the tip of the right tubal stump. A sprouting (*sp*) of the tubal mucosa is shown and also seedlings (*sd*) in the wall of the uterine cornu which have the same histologic structure as the sprouts.
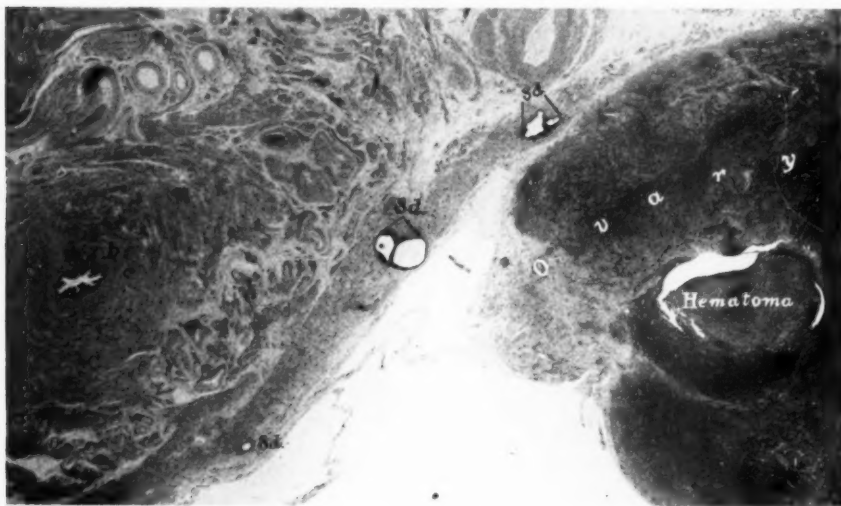
Fig. 27.—Photomicrograph (x 10) of the right tubal stump, adhesions between it and the ovary and a portion of the ovary. Seedlings with the same histologic structure as the sprouts and the seedlings shown in Figs. 25 and 26 are present in the adhesions. The lining of the ovarian hematoma has the same histologic structure as these. Evidence, just presented, indicates that the hematoma of the ovary is a seedling derived from the transplantation of tubal epithelium, but, at best, this evidence is only circumstantial.

dominal wall. The uterus was not curetted. The patient felt well for a year after the operation, when, during menstruation, she began to have pain and tenderness in the abdominal wall to the left of the scar. This increased in severity and duration. A nodule was first noticed by her three years after the operation.

This nodule seemed larger during menstruation and was very tender at that time. She was examined by me in September, 1926. The uterus was found to be fixed to the anterior abdominal wall and a definite tender nodule was felt in the left rectus muscle and apparently attached to the uterus. A preoperative diagnosis of endometriosis of the abdominal wall was made. The uterus and left tube and ovary were removed with the nodule attached to the left uterine cornu (Figs. 28 and 36). The nodule involved the left rectus muscle and was fused with the left uterine cornu at the site of the tubal sterilization (Fig. 37). The entire specimen was fixed in formalin and the course of the tubal stump and possible origin of the ectopic müllerian tissue was studied by sections cut in planes parallel to the long axis of the uterus. An endometriosis of the uterine cornu was found and also of the peritoneum, which had been sutured about the fundus of the uterus

Fig. 28.—Anterior view (x 2/3) of the uterus, left tube and ovary with a piece of the left rectus muscle which is fused to the surface of the left uterine cornu at the site of a previous tubal sterilization (Case 5). See Figs. 29, 35, and 36.

at the first operation. The endometrial elements had invaded the rectus muscle causing the nodule which could be felt in the abdominal wall. By carefully following the course of the tube beginning at its origin from the uterine cavity, it was found that an endometriosis of the uterine cornu had resulted from a direct extension of the traumatized tubal mucosa in the end of the severed tube (Fig. 29). The endometriosis of the uterine cornu was found to be continuous with that of the peritoneum adherent to it and also with that in the rectus muscle. It was impossible to follow the course of all of the endometrial elements in the specimen and, therefore, one cannot state that all of the endometrial tissue of the abdominal wall arose from a direct extension of the mucosa of the tubal stump, but some of them did. Grossly, an endometriosis also was present in the opposite uterine cornu, but microscopic sections were not studied, as unfortunately the specimen was lost.
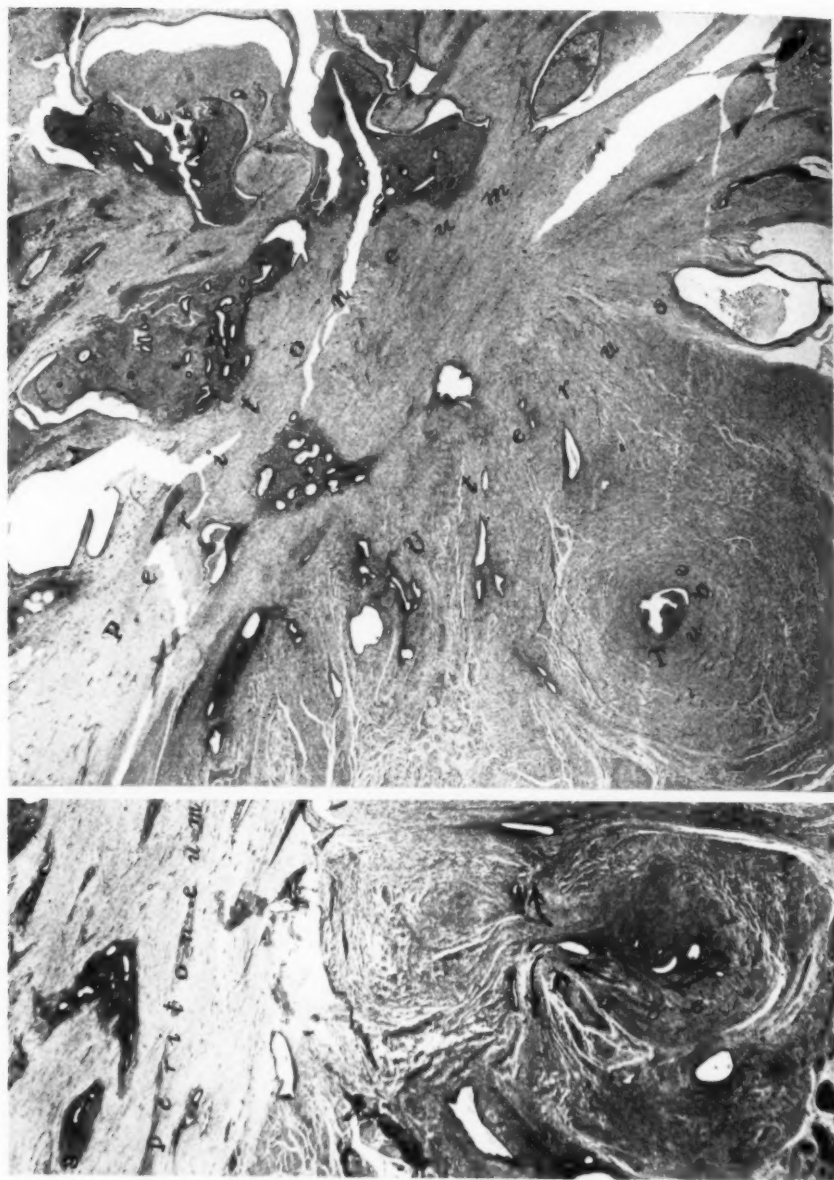
Fig. 29.—Two photomicrographs (x 10) from a series of cross-sections of the left uterine cornu and the nodule which was removed with a portion of the left rectus muscle (Figs. 28, 36, and 37).

The upper photomicrograph shows a portion of the left uterine cornu and also of the nodule which is fused with it at the site of the tubal sterilization. An endometriosis is present which has invaded both the uterine cornu, the peritoneum fused with the latter and the left rectus muscle above the peritoneum. The interstitial portion of the tube appears in cross-section. What is the origin of the endometriosis? The tube was followed in these cross-sections to the tip of the stump. Here, as shown in the lower photomicrograph, tubules of its mucosa (sprouts) have extended from the stump and have invaded the tissues about it and evidently caused the endometriosis shown in the preceding photomicrograph.

CASE 6.—Endometriosis of both uterine cornua and of the left rectus muscle, following ventrofixation of the uterus. Patient, aged forty-two (two children) had been operated on by me in 1923 for a weakened pelvic floor and retroverted uterus. The uterus was curetted, cervix amputated, pelvic floor repaired, appendix, left tube and ovary (cystic) removed, right tube severed at its uterine end and ligated and the fundus of the uterus fastened, extraperitoneally, to the anterior abdominal wall. Small endometrial implants were present in the culdesac. The patient felt well for over two years when she began to have pains during menstruation in the abdominal wall to the left of the scar. This gradually increased in severity and the tenderness persisted for two weeks after each menstrual flow. When examined by me in March, 1927, the uterus was found fixed to the abdominal wall and a definite tender nodule was felt in the left rectus muscle and apparently attached to the uterus. A preoperative diagnosis of endometriosis of the abdominal wall was made.

The uterus was removed with the nodule attached to the left uterine cornu (Fig. 30). The entire specimen was hardened in formalin. Sections of the

Fig. 30.—Anterior view (x 2/3) of the uterus with a nodule (End.) which is fused to the surface of the left uterine cornu at the site of a previous salpingectomy. This nodule was removed from the left rectus muscle (Case 6). See Figs. 32 and 33.

right uterine cornu with the nodule attached were cut in planes at right angles to the long axis of the uterus. An endometriosis was present in the right uterine cornu. By carefully following the course of the tubal stump, it was found that the endometriosis did not arise from a direct extension of the mucosa of the tubal stump, but some of it apparently arose from the mucosa of the severed tube which had been buried near the tubal stump (Fig. 31).

By carefully following the course of the left tubal stump, which had been buried in the uterine cornu after removing the tube, the direct extension of the tubal mucosa from the severed end of the tube into the tissues of the uterine cornu was found (Fig. 32 and 33). Endometrial tubules extended from this into the peritoneum which had been sutured about the fundus of the uterus and also into the left rectus muscle. As in the previous case, one cannot state that all of the misplaced endometrial tissue arose from the direct extension of the tubal mucosa, but some of it did. In these two cases the endometriosis of the abdominal wall arose from the pre-existing müllerian mucosa, namely, that of the traumatized tube and by direct extension.

CASE 7.—Endometriosis of the abdominal scar following salpingectomy for tubal pregnancy. In October, 1926, Dr. E. MacD. Stanton of Schenectady, sent me a specimen of endometriosis of the abdominal scar which he had removed, and included with it a history of the case and his operative findings. The patient had two previous operations, the first an appendicectomy twelve years before and the second an operation for tubal pregnancy five years later. A nodule appeared in the lower end of the abdominal scar three years after the last operation. This nodule became painful and swollen during menstruation and at the last two menstrual periods, blood was discharged from it. On examination a bleeding fistula with induration about it was found. At operation, by Dr. Stanton, the scar of the previous incision was incised above the mass and the peritoneal cavity opened. The uterus was not adherent to the abdominal wall, nor was there any
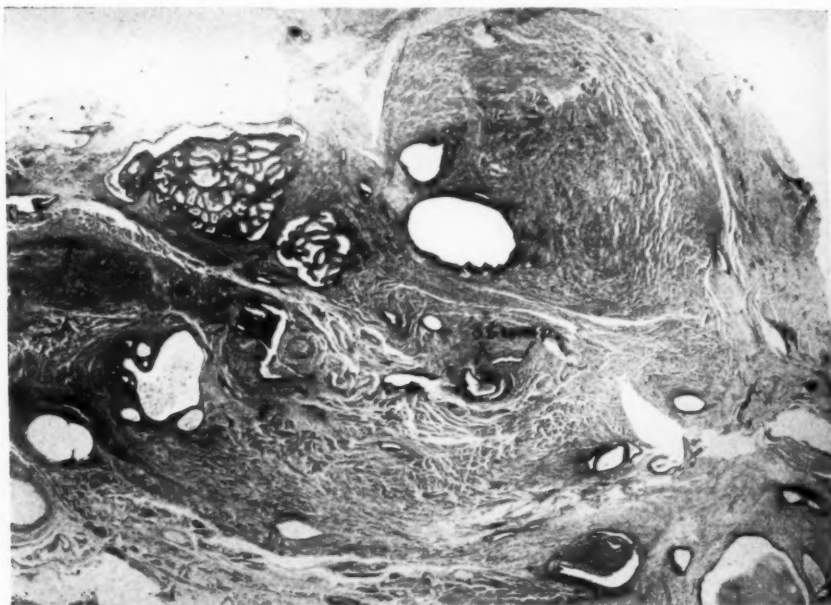
Fig. 31.—Photomicrograph (x 10) from a series of longitudinal sections, in a perpendicular plane, of the right uterine cornu, the seat of a previous tubal sterilization (Fig. 30). The very tip of the proximal tubal stump is shown in cross-section without any sprouts arising from its mucosa. The stump of the distal portion of the tube appears in longitudinal section with evidence that some of the endometriosis in this photomicrograph might have arisen from the direct outgrowth of its mucosa into the surrounding tissues.

demonstrable indication of peritoneal endometriosis. A typical endometriosis (Fig. 34 and 38) was present in the subcutaneous tissues of the laparotomy scar and was not connected with the peritoneal cavity. Its histologic structure was identical with that of the previous ones which arose from the tubal mucosa by direct extension. This, I believe, also arose from müllerian mucosa but by transplantation, just as similar lesions arise in the tissues about the tubal stump after salpingectomy.

THE REACTION OF POSTSALPINGECTOMY ENDOMETRIOSIS TO MENSTRUATION AND PREGNANCY

Postsalpingectomy endometriosis arises either from sprouts growing out from the mucosa of the tubal stump or as seedlings in and

about the tubal stump or at a distance from it. These seedlings have the same histologic structure as the sprouts, but are not continuous with them and occur in situations, where we know tubal epithelium easily may have been transplanted at the original operation. However convincing the evidence may be that some of these seedlings arise from the growth of transplanted tubal epithelium, this evidence, at best, is only circumstantial.

The direct endometriosis, that arising from an outgrowth of the mucosa of the tubal stump, is of two types: tubal and uterine. In those of tubal type the mucosa retains the structure of the tube from
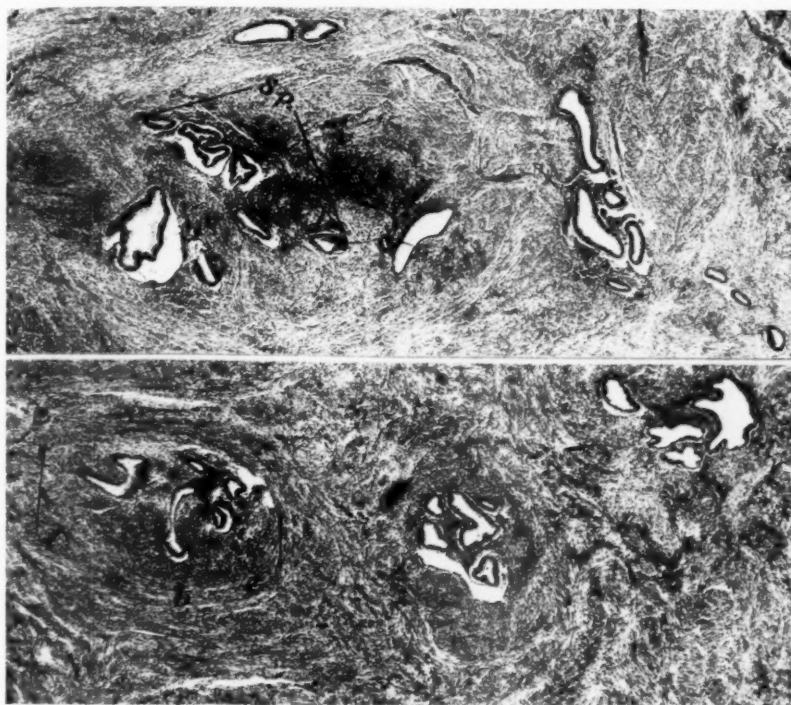
Fig. 32.—Two photomicrographs (x 25) from a series of longitudinal sections, in a horizontal plane, of the left uterine cornu which was fused with the nodule involving the left rectus muscle. Same case as the preceding. The left tube and ovary had been removed and the tubal stump buried in the uterine cornu.
The lower photomicrograph shows the distal end of the tubal stump with its lumen filled with hyperplastic (activated) tubal mucosa.
The upper photograph shows the mucosal sprouts which have grown out from the activated mucosa of the tubal stump and have invaded the tissues of the uterine cornu.

which it came. In those of uterine type the misplaced tubal mucosa is activated to simulate the structure of the uterine mucosa, even that arising from tubal stumps ligated distal to the uterine cornu. In some instances this postsalpingectomy endometriosis of uterine type does not react to menstruation, but in others it apparently does, as shown by evidence of hemorrhage in these misplaced uterine cavities of tubal origin. In the three cases with typical endometrial cysts

or hematomas in the ovaries arising from the direct invasion of that organ by tubal mucosa growing out from the tubal stump, the cysts were not only lined by endometrium-like tissue, but were also filled with blood. Some may claim that the blood in these ovarian hematomas was not of menstrual origin. In the two patients with endometrial "tumors" involving the recti muscles, these tumors arose from the direct extension or outgrowth of the mucosa of the tubal stump into the uterine cornu and thence to the anterior abdominal wall. These nodules not only contained misplaced "uterine" cavities lined by endometrium and filled with blood, but were very tender and seemed larger during menstruation.

Three of the patients with postsalpingectomy endometriosis were operated upon for tubal pregnancy. The first operation in two of

Fig. 33.—Photomicrograph (x 10) of the section shown in the upper photomicrograph of Fig. 32. A portion of the uterine cornu occupies the right half of the photomicrograph and the nodule which had involved the rectus muscle occupies the left half. The endometriosis of the uterine cornu which arose from the sprouting of the mucosa of the tubal stump can be followed by direct extension into the nodule fused with the uterine cornu. The endometriosis of the abdominal wall evidently arose from tubal mucosa by the direct extension of sprouts from the traumatized mucosa of the tubal stump.

these cases had been a unilateral salpingo-oöphorectomy for salpingitis and in the third patient a ventrofixation of the uterus with attempted tubal sterilization.

In the first two cases an endometriosis (of tubal origin) of both uterine cornua probably was present at the first operation. There was no evidence of a decidual reaction in this misplaced tubal mucosa of the uterine cornua, nor was it present in the mucosa of the uterine cavity in either case.

In the third patient an extensive endometriosis was present in both uterine cornua resulting from an outgrowth or sprouting of the

mucosa of the stumps of the severed tubes. It was impossible to ascertain the exact situation of the ectopic pregnancy, whether it was primarily tubal or primarily embedded in an ectopic uterine cavity in the lesion of the left uterine cornu. The endometriosis of tubal origin in both uterine cornua showed a marked decidual reaction (Fig. 12), as did also the mucosa of the uterine cavity. Sections of both tubes showed no decidual reaction in their mucosa.

We must conclude that postsalpingectomy endometriosis arising from the sprouting or outgrowth of the mucosa of the tubal stump, sometimes is activated to form histologically typical uterine mucosa and that this mucosa may not only menstruate, but during preg-
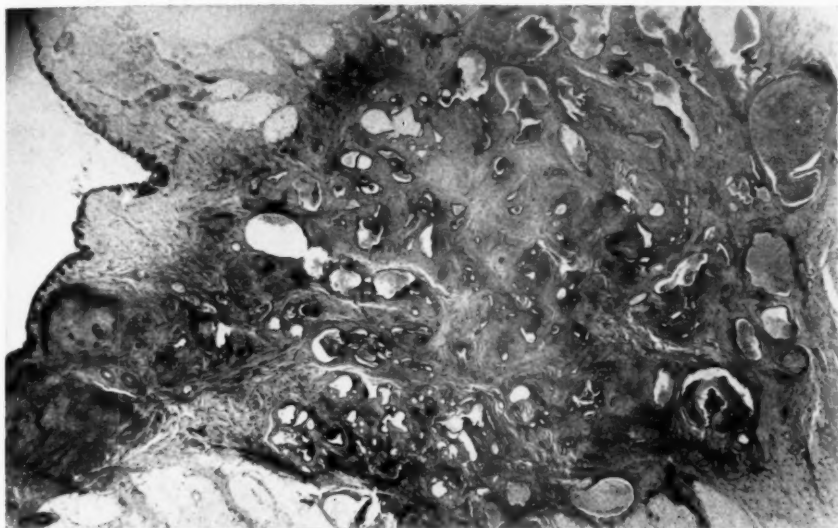
Fig. 34.—Photomicrograph (x 5) of a section of a subcutaneous endometriosis of the abdominal scar following salpingectomy (Case 7). The nodule is above the fascia of the abdominal wall. It is not connected with the peritoneum nor was the uterus adherent to the abdominal wall. It has the same histologic structure as that of the cases of endometriosis of the abdominal wall, just described. It was shown that the latter arose from tubal mucosa by direct extension. I believe that this also arose from tubal mucosa, but by transplantation.

nancy it may show a decidual reaction. We would expect that endometriosis arising from the transplantation of tubal mucosa might do the same.

THE CLINICAL SIGNIFICANCE OF POSTSALPINGECTOMY ENDOMETRIOSIS

These studies demonstrate that endometriosis frequently follows salpingectomy and tubal sterilization. They also show that it is usually of slight extent and only of scientific interest. On the other hand, in some instances, it is so situated and is sufficiently extensive as to cause discomfort and necessitate another operation for the relief of the patient. Many patients who have had conservative surgery for the relief of salpingitis and its sequelae have discomfort and pain following these operations which are usually attributed to

postoperative adhesions. In some of these cases the adhesions are the result of a postsalpingectomy endometriosis.

Postsalpingectomy endometriosis usually arises from sprouts growing out from the traumatized tubal mucosa, such as the mucosa protruding from the end of the severed tube, that resulting from clamping and ligating the tube and from transfixing the lumen of the tube with a ligature. Evidence, of necessity only circumstantial, indicates that endometriosis also arises from uterine and tubal mucosa transplanted by the surgeon.

The prophylaxis of postsalpingectomy endometriosis lies in the more careful selection of cases in which the uterus is retained after salpingectomy and in the more careful operative technic in the removal of the tube. Since we have appreciated the latter, it has been our
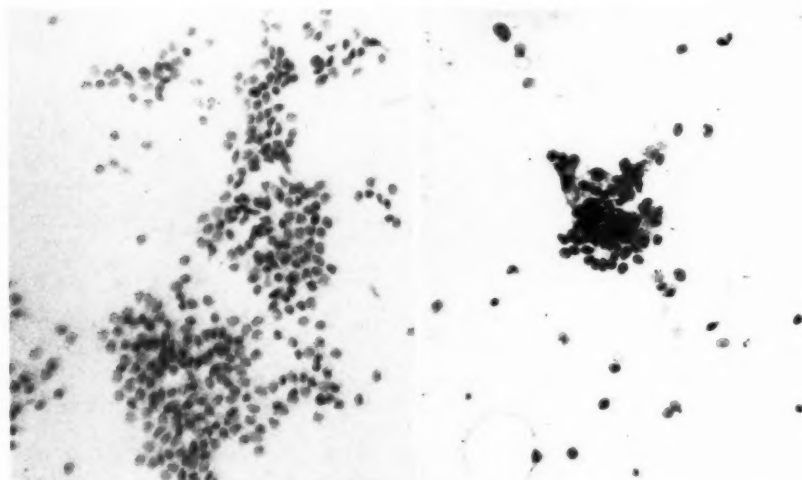
Fig. 35.—Two photomicrographs (x 130) of smears made from a small bit of wet gauze held in a clamp and introduced into the peritoneal cavity.

The first was obtained from gauze introduced into the pelvis between the posterior surface of the uterus and coils of intestines. Probably all of the cells shown in this photomicrograph are mesothelial cells. The second was obtained by carefully exposing the fimbriated end of the tube and drawing the gauze across its surface. The cells differ from those shown in the preceding illustration and are probably epithelial cells. In every abdominal operation many mesothelial cells must be transplanted in the abdominal wound. Occasionally epithelium from the fimbriated end of the tube is transplanted into the abdominal wound by withdrawing gauze which came in contact with the tubal fimbriae, even in appendicectomy. If tubal epithelium transplanted during salpingectomy grows, it might also grow when transplanted from the fimbriae of the tube.

custom to sever the tube with a cautery and to bury the stump in the uterine cornu without clamping it or piercing it with the needle carrying the suture.

ENDOMETRIOSIS OF THE ABDOMINAL SCAR FOLLOWING OPERATIONS OTHER THAN SALPINGECTOMY

Endometriosis in this situation has been reported following all abdominal operations on the pelvic organs. (See cases collected by Nicholson and others.) In some of these, neither the lumen of the

tube nor the uterine cavity has been exposed, nor had the latter been pierced by a needle carrying a suture. Cases also have been reported following appendicectomy in women.

It has been shown that when an abdominal operation has been preceded by a curettage, blood containing bits of uterine mucosa, at times, escapes from the uterine cavity through the lumen of the tubes, and that this "cellular spill" is increased by the operative manipulation of the uterus. In such operations these bits of uterine mucosa might be transplanted in various parts of the operative field, including the abdominal wall. Should the abdominal operation not be preceded by a curettage, the operative handling of the tubes might transfer epithelium from the fimbriae to other parts of the field of operation. Peritoneal endometriosis might have been present in some of these cases at the first operation.

How could tubal epithelium possibly be transferred to the abdominal wound in appendicectomy? We have studied this particular problem in the following manner. In pelvic operations, in which the appendix was removed, care was exercised not to touch its tip. After its removal smears were made by drawing the tip of the appendix over the surface of glass slides. Similar smears were made from the fimbriated ends of tubes. Some of these preparations were examined without fixation and staining. Others were stained with methylene blue and others were fixed in Zenker's or in Helly's solutions and stained with hematoxylin and eosin. Many cells, isolated and in clumps, were found in these preparations. Obviously smears from the appendix should contain mesothelial cells and those from the fimbriae of the tubes both mesothelial and epithelial cells. A comparative study of the slides from the two sources should enable one to distinguish the mesothelial from the epithelial cells. As a further control, tubes and uteri were carefully split open and scrapings were made with a sharp knife or a small piece of gauze held in a clamp from the surfaces of the mucosa thus exposed. These were spread on slides and treated as were the previous ones. We have been studying this problem for over a year and have examined many slides from many patients and have not yet found a satisfactory method of always distinguishing these two cells, especially when they are isolated. Nevertheless, we can sometimes be sure of our findings and have shown that tubal epithelium may be transferred to a glass slide by brushing the fimbriae over the surface of the slide. In like manner tubal epithelium could be transferred by the surgeon to the abdominal wound or any other part of the operative field, if he handled the fimbriated end of the tube.

The second phase of the study of the problem was conducted in the following manner: At operation a small wet piece of gauze, held in a clamp, was inserted in the pelvis between the posterior surface

of the uterus and the coils of intestines and withdrawn. Smears on slides were made from these. We were astonished at the large number of mesothelium cells found, thus indicating the trauma caused by inserting gauze into the peritoneal cavity, even a small piece of wet gauze. After carefully exposing the tubes, similar gauze bits were rubbed against their fimbriae and smears made from these. The histologic findings (Fig. 35) were identical with those obtained by brushing slides with the tubal fimbriae. Similar observations were made in appendicectomies through a McBurney incision.

These observations showed that gauze introduced into the peritoneal cavity in any form, as a tampon or bit in a sponge stick, removes a large amount of the mesothelium from the surface of the organs and structures, with which it comes in contact and that in every operation some of this mesothelium must be transferred to the tissues of the abdominal wound on removing the gauze. These observations also show that should the gauze come in contact with the fimbriae of the tube, even in appendicectomies through a McBurney incision, tubal epithelium will, at times, be transferred to the abdominal wound on removing the gauze. The surgeon, therefore, always transplants a large number of mesothelial cells into the tissues of the abdominal wound in every abdominal operation and sometimes transplants tubal epithelium. We have already presented evidence indicating that tubal epithelium transplanted by the surgeon in salpingectomy may, at times, give rise to endometriosis. Why should not tubal epithelium transplanted by gauze or any other operative procedure from the fimbriae of the tube do the same?

The presence of endometrial tissue in laparotomy scars was discussed by Heaney[10] at the 1925 meeting of the American Gynecological Society. He collected 29 cases from the literature. Seven of these followed operations in which the pregnant uterus had been opened by intent or accident. He added 2 of his own to the latter. Abstracts of these cases may be found in his paper. Danforth[11] reported an additional case at the same meeting.

If endometrial tissue in laparotomy scars after the incision of the pregnant uterus develops from bits of uterine mucosa transplanted

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Fig. 36.—Posterior view (natural size) of the left uterine cornu with a piece of the rectus muscle fused with the latter at the seat of tubal sterilization (Case 5). See Figs. 28, 29, and 37. The fundus of the uterus was fixed extraperitoneally to the anterior abdominal wall. Peritoneal implants (*imp.*) are present beneath the tube and possibly arose from the tubal sterilization when the tube was severed close to the uterus and its ends ligated.

Fig. 37.—Cross-section (natural size) of the uterine cornu and a portion of the rectus muscle which was fused with it (Figs. 28 and 36). An endometriosis is present in the uterine cornu and also in the rectus muscle (Fig. 29). Cavities in the latter, dilated with blood, are brown in contrast with the red muscle.

Fig. 38.—Cross-section (natural size) of an abdominal scar with endometriosis in the subcutaneous fat (Case 7). Section was taken either just below or above the bleeding fistula. Evidence of the latter can be seen in the pigmented skin. The gross appearance of and the histologic structure (Fig. 34) of the endometriosis in this case were identical with that of the preceding. The latter arose from tubal mucosa by direct extension. The latter, I believe, also arose from tubal mucosa but by transplantation.
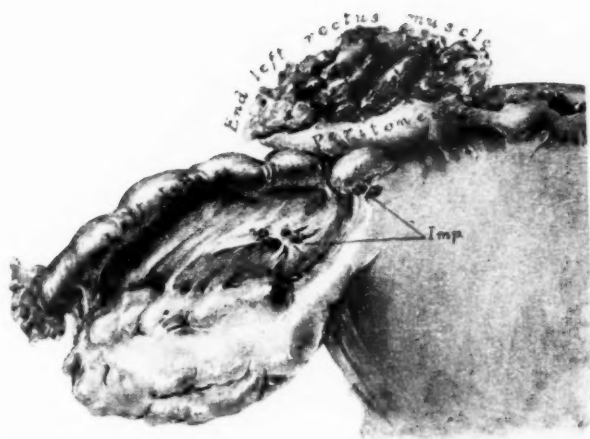
FIG. 36
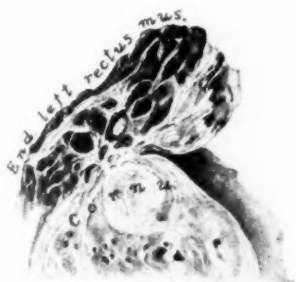
FIG. 37

FIG. 38
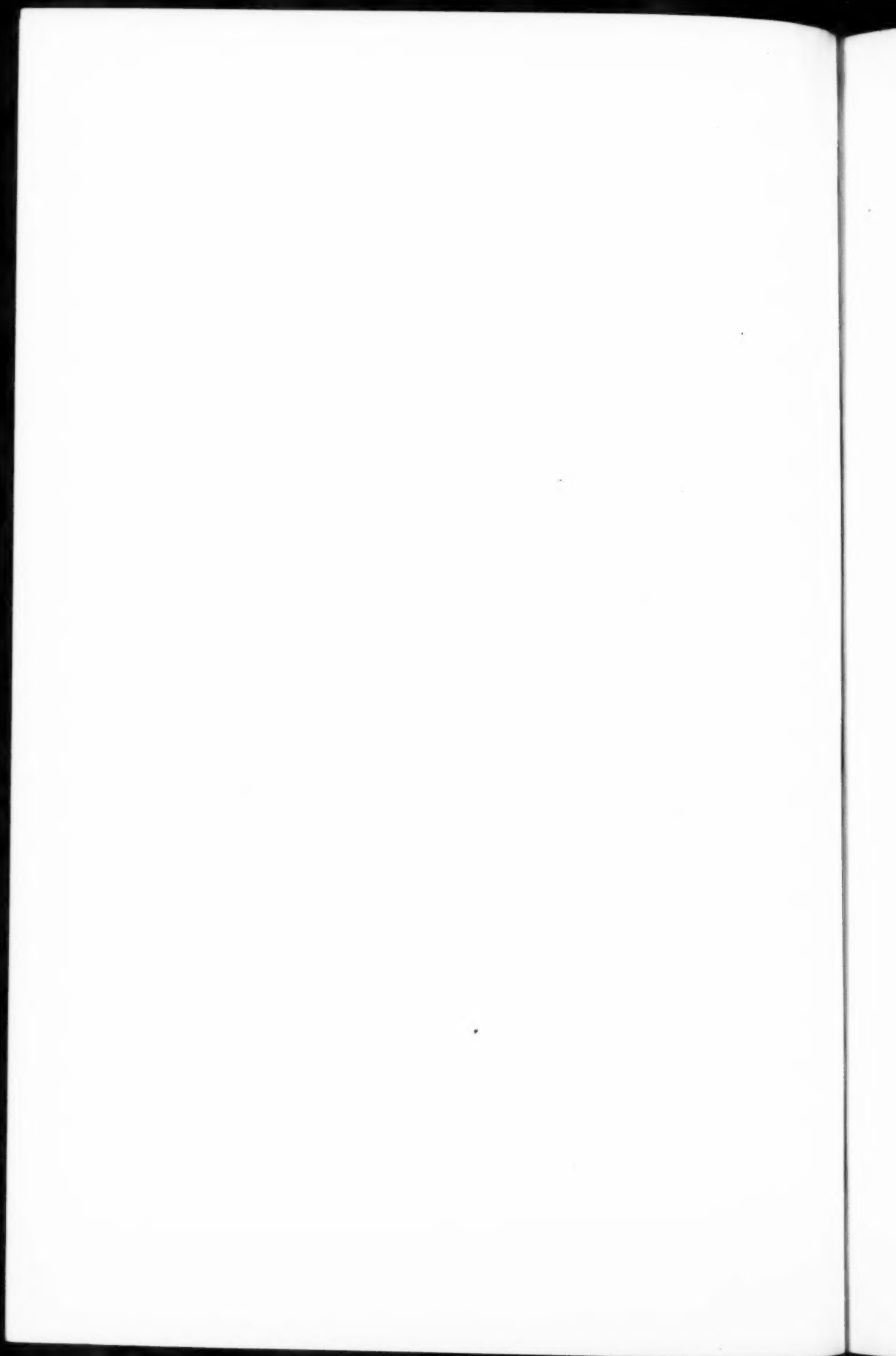
by the surgeon, we would expect often to find a similar condition in
the uterine scars and in near-by pelvic structures following these
operations. Schwarz[12] has recently reported an additional case of
endometrial tissue in the abdominal scar following cesarean section.
He states that in his study of the cesarean scar of the human uterus,
he has found endometrial tissue along the line of incision in two in-
stances. In his experimental study of the cesarean scar in the guinea
pig, endometrial tissue was found in several cases along the line of
incision as well as on the peritoneal surface of the uterus. Circum-
stantial evidence would indicate that the müllerian mucosa found in
laparotomy scars after cesarean section arose from the growth of
uterine mucosa transplanted by the surgeon and not from tubal epi-
thelium. We have shown that tubal mucosa injured by salpingec-
tomy may invade the tubal stump and structures adherent to it and
that this misplaced müllerian mucosa may assume the structure of
the uterine mucosa and even its function. It is possible that in some
of the cases of endometriosis of laparotomy scars following cesarean
section, the müllerian mucosa in the scars was of tubal and not of
uterine origin, as in the cases where the uterine cavity was not
opened.

POSTOPERATIVE VAGINAL ENDOMETRIOSIS

Peritoneal endometriosis is found more frequently in the posterior
culdesac than in any other situation. Based on the serosal theory
for the origin of this condition, the peritoneum of the posterior cul-
desac must be richer in potential müllerian mucosa than any other
portion of the peritoneum. If endometriosis of laparotomy scars
arises from the differentiation of peritoneum included in that scar,
and especially the peritoneum of the abdominal wall which appar-
ently is relatively poor in potential müllerian mucosa, we would cer-
tainly expect frequently to find an endometriosis of the vaginal vault
following panhysterectomy or any other operation by which bits of
the peritoneum of the posterior culdesac might be transplanted in
the vaginal wound. If the endometriosis of laparotomy scars arises
from the growth of bits of uterine mucosa transplanted by the sur-
geon, we would expect frequently to find a similar condition in the
vaginal scars after labor and after a repair of the pelvic floor which
has been preceded by a curettage of the uterus. We have been study-
ing the small cysts frequently found in vaginal scars and have en-
countered only one with a histologic structure similar to that of
ectopic müllerian mucosa.

The rarity of possible postoperative endometriosis in vaginal scars
fails to support either the serosal or the mucosal origin of endo-
metriosis of laparotomy scars. Are vaginal tissues ill suited to the
growth of müllerian mucosa? Endometriosis of the posterior vaginal
vault frequently arises from the direct extension downward of similar
tissue in the culdesac.

Tubal epithelium is much more frequently transplanted in abdominal than in vaginal wounds. Tubal epithelium apparently plays a large part in the etiology of endometriosis of abdominal scars. Could it be possible that tubal epithelium can be more successfully transplanted than uterine?

BEARING OF THE PRESENT STUDIES ON THE ORIGIN OF PERITONEAL ENDOMETRIOSIS OTHER THAN POSTOPERATIVE

The evidence indicating that peritoneal endometriosis, at times, arises from the implantation of müllerian epithelium escaping through or from the tubes may be summarized as follows:

1. It occurs in women and not in men.

2. It is an acquired lesion and usually (possibly always) develops during the menstrual life of women and most frequently in the latter half of that life.

3. Experiments in the autotransplantation of bits of müllerian mucosa in the lower animals by Jacobson and others show that it may be successfully transplanted to the peritoneum of these animals.

4. The study of postoperative endometriosis in women shows (or at least suggests) that tubal and uterine epithelium may be successfully transplanted by the surgeon.

5. The study of endometrial tissue in the ovaries suggests that this tissue may spread to the peritoneum by the implantation of epithelium which escapes from the ovary both through the perforation (menstrual) of endometrial cysts and also the menstrual reaction of endometrial tissue on the surface of the ovary. This evidence is purely circumstantial, but, to me, it is most convincing.

6. Peritoneal endometriosis often occurs without any discernible endometrial tissue in the ovaries, the latter, therefore, not being essential in the development of the peritoneal lesion.

7. One of the outstanding features of patients with peritoneal endometriosis is that the tubes are usually patent. In 342 patients with peritoneal lesions containing endometrium-like tissue (other than postoperative), encountered by me in the last six years, both tubes appeared to be patent in 330. A unilateral hematosalpinx was present in 3 and bilateral hematosalpinx in 4. Patent tubes apparently increase the incidence of peritoneal endometriosis and the relatively large number of patients with hematosalpinx must be of some significance. In the cases with occlusion of both tubes, the peritoneal lesions might have been present prior to the closure of the fimbriated ends of the tubes.

8. The peritoneal lesions often occur in situations and under conditions indicating their origin from material escaping from or through the patent tubes.

9. The present study shows that the traumatized mucosa of the tubal stump (after salpingectomy) may not only invade the stump but also any structure adjacent or adherent to it and give rise to the lesions of peritoneal endometriosis, including typical endometrial cysts or hematomas of the ovary.

10. These same studies show that this misplaced tubal mucosa may assume the structure of the uterine mucosa. Therefore, many of the endometrium-like lesions of peritoneal endometriosis could be of tubal and not of uterine origin.

11. It has been shown that bits of the uterine mucosa, set free by curettage, may be carried by blood escaping from the uterine cavity into the tubes.

12. It has also been shown that, during menstruation, blood may escape from the uterine cavity into the tubes and that this blood may contain bits of the uterine mucosa.

13. We have evidence[13] indicating that bits of the uterine mucosa may escape into the venous circulation of the uterus during menstruation and become implanted in the venous sinuses of the uterine wall.

14. Since peritoneal endometriosis develops during the menstrual life of women and as the menstrual reaction is one which often causes a dissemination of bits of uterine mucosa and possibly also of the tubal mucosa, it is natural to look upon it as an important factor in the dissemination of müllerian epithelium into the peritoneal cavity.

15. Tubal epithelium might readily escape from the tubal fimbriae independent of menstruation.

16. The evidence thus far obtained shows that peritoneal endometriosis might arise from the implantation of both tubal and uterine epithelium.

17. The present studies support this theory and emphasize the origin of peritoneal endometriosis from the implantation of tubal epithelium, but do not exclude its origin from other sources.

THE BEARING OF THE PRESENT STUDIES ON THE ETIOLOGY OF ENDOMETRIUM-LIKE TISSUE IN THE OVARIES OTHER THAN POSTOPERATIVE

These studies demonstrate that the traumatized mucosa of the tubal stump may, by direct extension, invade the adjacent ovary and give rise to typical endometrial cysts or hematomas of that organ (3 cases) and in one instance endometrial tissue on the surface of the ovary apparently arose from the implantation of tubal mucosa from the tubal stump. As has been emphasized, the tubes are usually patent in patients with endometrial tissue in the ovaries and the endometrial lesions on the surface of the ovaries nearly always occur on the lateral and under surfaces of that organ in situations readily contaminated by material escaping from the patent tubes and where that

material would be protected and held in place, thus favoring the "taking" of the graft. Circumstantial evidence indicates that, at times, endometrial tissue in the ovaries arises from the implantation of epithelium escaping from and through the tubes. Because a variety of epithelial structures arises in the ovaries, it is natural to assume that the endometrium-like tissue in that organ, at times, might arise from other sources than the implantation of epithelium escaping from and through the tubes.

These studies support the theory that endometrium-like lesions in the ovaries may arise from the implantation of müllerian epithelium escaping through or from the tubes. It emphasizes the part played by tubal epithelium, but it does not exclude its origin from other sources.

SUMMARY

1. Endometriosis was found in and about the tubal stumps in 30 of 36 patients who had had a previous salpingectomy or tubal sterilization.

2. Postsalpingectomy endometriosis usually arises from sprouts growing out from the traumatized mucosa of the tubal stump. These sprouts may invade not only the wall of the tube but also the uterine cornu and any structure adjacent or adherent to the stump, such as the tissues of the broad ligament, the ovaries (3 cases), and even the abdominal wall (2 cases).

3. The misplaced tubal mucosa in these lesions, at times, retains its original structure and at other times assumes both the structure and function of the uterine mucosa including its reaction to menstruation and pregnancy. It presents the histologic picture of endometriosis of nonoperative origin including typical endometrial cysts or hematomas of the ovary.

4. In the various operative procedures, incident to salpingectomy, bits of tubal and uterine mucosa may be transplanted by the surgeon both in the immediate field and also in remote ones. Endometriosis, with the same histologic structures as that present in sprouts, springs up as seedlings in situations where tubal and uterine epithelium might have been sown. It is natural to assume that some of these seedlings sprang from epithelium transplanted by the surgeon.

5. If tubal epithelium transplanted during salpingectomy grows, it should also grow if transplanted during other operations than salpingectomy and by other means than operations.

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CYCLICAL AND OTHER VARIATIONS IN THE TUBAL EPITHELIUM

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UP TO 1908 the expression "menstrual cycle" meant little more than the periodic recurrence of a physiologic hemorrhage from the uterine cavity. In that year Hitschmann and Adler, in one of the really epoch-making contributions to gynecologic literature, demonstrated that the endometrium exhibits a cycle of histologic changes which involve all three of its constituent elements, i.e., the epithelium, the glands, and the stroma. Even before this a good start had been made in the demonstration of a definite histologic cycle in the ovary, chiefly in the pioneer work of Fraenkel and others upon the life cycle of the corpus luteum. The attempt to correlate the two cycles was a natural sequence. From a histologic and chronologic standpoint this offered little difficulty, but the physiologic interrelationships of the two cycles constitute a problem which, in spite of the great advances of recent years, still remains unsettled.

The demonstration that the vaginal mucosa of the lower animals likewise undergoes a regular cycle of histologic changes culminated in the discovery by Stockard and Papanicalaou, in 1917, that this vaginal cycle can be easily followed by examining the cell composition of vaginal smears. This simple test has enormously facilitated the study of the sex cycle in laboratory animals.

Whatever the underlying sex impulse may be, it obviously affects very profoundly all tissue derived from the müllerian ducts. Only in the cervix and the tube does it remain to describe a histologic cycle comparable to that in the uterus, ovary, and vagina. It is true that in the human being the vaginal cycle has not as yet been very satisfactorily demonstrated. Indeed, we know of only one adequate study of this subject which has as yet been made, that of Diercks in 1927.

With regard to the cervix, also, no evidence has as yet been adduced to indicate that it participates in the constantly changing histology of the genital mucosa, although one would expect that it must possess some sensitivity, however vestigial, to the sex stimulus. In the course of the investigations we are to describe in this paper, we have

incidentally had occasion to study many cervices removed at different phases of the cycle, but have not been able to detect any changes suggesting a cyclical influence.

The present communication deals with the study of a rather large number of tubes, in an effort to describe perhaps more fully than has hitherto been done any histologic cycle of changes which might be demonstrable in the tubal epithelium and to correlate this, if possible, with the now clearly defined cycle which occurs in the endometrium. Moreover, we have thought it worth while to study, in a small series of cases at least, the tubal epithelium in patients with certain disturbances of ovarian function, particularly functional uterine bleeding. This seemed of especial interest in that this functional disorder is associated with a characteristic histologic change in the endometrium (hyperplasia of the endometrium). Finally, we have endeavored to study the characteristics of the tubal epithelium in fetal life, in childhood, in senility, and during pregnancy.

Heretofore the possible participation of the tube in the menstrual process has been discussed almost entirely from the standpoint of the menstrual bleeding alone, and much has been written on both sides of the question of whether or not the tubal mucosa exhibits a physiologic bleeding, like that of the endometrium. We shall have occasion to touch upon this point later, but in this paper our chief purpose is to present observations which emphasize the fact, so well illustrated in the endometrium itself, that bleeding is only one of the manifestations—much less fundamental than some of the others—characterizing the menstrual phenomenon.

HISTORICAL

In view of the paucity of studies on this subject in the English language, it seems worth while to submit a fairly complete survey of its historical development, for the benefit of subsequent workers. The literature up to 1908 is thoroughly reviewed by Schaffer, to whose article we are indebted for a number of citations from publications which would otherwise have been inaccessible to us.

The traditional description of the tubal epithelium, and the one found in almost all modern textbooks, is of a single layer of ciliated columnar epithelium. This statement is so incorrect, if made unqualifiedly, that it is difficult to see how it has been perpetuated, especially in view of the fact that its incorrectness was pointed out by Frommel as far back as 1886. In a short communication before the German Gynecological Society this observer called attention to the fact that the tubal epithelium is made up of two chief types of cells, one ciliated, and the other nonciliated and apparently secretory. He also described another type, a rod-like cell, with a flat compressed nucleus and no cytoplasm. This is undoubtedly the cell which was later spoken of as the "Stiftchenzelle," as will be discussed later in this paper. Frommel's first studies were made upon the tubes of cats, but he extended them also to other animals (dogs, sheep, monkeys).

From time to time since Frommel's publication, other authors have corroborated his observations, without apparently making any great impress upon traditional belief. In 1890 Nicolas, for example, reported studies upon rabbits, guinea pigs, and cats, in all of which he found the two types of epithelium described by Frommel. He believes that the nonciliated cells are in the majority, and that they exhibit a considerable degree of polymorphism. This latter observation is of interest in view of the fact that not a few subsequent observers look upon this polymorphism as an evidence of transformability of one type to another.

Woskressensky (1891) was so impressed with the probable secretory importance of the nonciliated epithelium that he performed double ligation of the tubes in rabbits and other animals, interpreting the exudate between the ligatures as an accumulation of the secretion of these cells. This interpretation, it need scarcely be said, was not a justifiable one.

Tréche (1893) studied human autopsy material with essentially the same findings as Frommel. Incidentally, he concluded that cilia are present in the tube but not in the uterus, an observation which we believe places him distinctly ahead of his time, inasmuch as we have likewise come to believe that the time-honored description of cilia in the human endometrium is probably incorrect. We are studying this problem at present.

Herman (1894) believed that the polymorphism of the secretory cells described by Frommel is merely an evidence of the degenerative and regenerative changes constantly taking place, an observation which again strikes a distinctly modern chord.

Sobotta's studies (1895) were made upon the tubes of mice. He found cilia to be present in the distal portion of the tube alone, an observation which is not substantiated by later investigations. In the human being, our own work has convinced us that cilia are present throughout the length of the tube. More clearly than any of his predecessors, Sobotta called attention to the fact that the nuclei often project beyond the epithelial border, appearing to rest on the cilia of adjoining cells. This, as we shall see, is a very common and very striking picture in the human tube as well. He describes also the peculiar cells with compressed nuclei, which he suggests may be wandering leucocytes squeezing their way between the cells. This view is later shared by Bindi (1905), who adds the interesting suggestion that they may be concerned with the removal of masses of degenerated spermatozoa.

Mandl (1897) did not believe that the available evidence justified the view that a definite secretion was given into the lumen of the tube by the so-called secretory cells. Janot (1898) asserted that the cilia of the tubal mucosa disappear in pregnancy. This observation, as we shall show from our own material, is incorrect.

Chrobak and Rosthorn (1900) stated that the secretory cells are found especially in the ampulla of the tube, while the isthmus shows a predominance of the ciliated cells.

An excellent contribution was that of Voinot (1900), especially in that his material was derived from the operating room, or else was well fixed soon after death. He studied tubes from patients of all ages, and from all phases of the menstrual cycle, as well as from cases of pregnancy. Moreover, his sections were made from various parts of the tube (intramural, isthmus, ampulla, and fimbriated extremity). He found cilia absent during intrauterine life, though appearing in slight number just before birth. Up to the age of puberty he found two main types of cells, and, like Nicolas, he described various transition forms among the nonciliated cells. Among the latter he includes the "Stiftchenzellen" or "Schaltzellen." Cilia he found rare in the intramural portion, where the epithelium is of

rather regular cylindric type, with few intercalary cells. Chiefly nonciliated cells are found in the isthmus and ampulla, in the latter often forming tuft-like masses at the top of the folds. In the fimbriated extremity, finally, he found the ciliated cells predominating, with considerable variation in morphology.

During reproductive life he found the cilia greatly increased in number. In the interstitial portion and the fimbriated extremity the cells are almost all ciliated, while in the remainder of the tube cilia are found chiefly at the bases and sides of the folds. The nonciliated cells are found chiefly at the tips of the folds. This arrangement Voinot believes to facilitate the passage of the ovum, which, being taken up by the cilia at the fimbriated end, enters a gutter between two adjacent folds. This groove is covered over by a roof of nonciliated cells, so that the ovum cannot readily turn aside. It is therefore pushed along to the interstitial portion, where cilia again are present in large numbers, so that it is propelled into the uterus. Interesting as these observations are, they do not agree with the results of others, or with our own findings.

Voinot made no effort to describe cyclical changes related to menstruation, for even the cycle in the endometrium was then unknown. However, in the discussion of tubes removed at menstruation, he speaks of a marked proliferation of the epithelium. In pregnancy he found the cylindrical cells to become cuboidal or flattened, only when they lie over areas of decidual formation. Finally, the study of tubes from senile women (ages sixty to ninety-five years) showed the epithelium to be cuboidal or flattened, except in the interstitial portion, where it is still cylindric. Cilia may be retained even when the epithelium has become much flattened.

The studies of Gurwitsch (1901), made upon dogs, were concerned chiefly with the relation between the cell body and the basal granules. The latter, he states, are of dumb-bell shape. Incidentally, he does not believe that the epithelium of the tube secretes, but that the so-called secretory cells are to be interpreted as developing ciliated cells.

The first American contribution to the subject was made in a short discussion by Gage in 1904. This investigator found that in young mammals the tube is lined by a cylindrical epithelium, which is chiefly nonciliated, though some ciliated cells are present. In the bat and mouse cilia were found at the fimbriated ends of the tubes.

Linari (1904), on the contrary, found the epithelium to be chiefly ciliated, although some secretory cells were present. Unlike Voinot, moreover, he found the cilia most abundant on the tips of the folds, and the secretory cells between the folds. He calls attention to the great rarity of mitoses in the tubal epithelium, an observation which we can readily endorse from our own work. He thinks this fact would indicate that very few tubal cells are lost.

Gianelli's (1904) studies yielded conclusions much like those of Linari. In addition to human tubes he studied those of dogs, sheep, cows and pigs. He thinks that the ciliated and nonciliated cells are closely related, and describes transition forms. He found the secretory cells indifferent to all the stains tried. They occur in all parts of the tube, although they become less abundant toward the fimbriated end.

The paper of Hörmann (1907), while devoted primarily to a study of the connective tissues of the tube, is of interest to us in that it discusses the nature of the so-called ''peg'' cells. Hörmann takes issue with von Ebner, who had suggested that these cells might be of connective-tissue type, and considers them to be secretory cells which have emptied themselves and become flattened out.

One of the most important contributions to the subject was that of Schaffer, in 1908. As already mentioned, this author presented an extremely complete his-

torical survey of the whole question. He found that the proportion and character of the secretory cells differs in different animal species, as well as in different animals of the same species, and that these differences depend chiefly upon which portion of the tube is studied and what phase of the sexual cycle is represented. In a general way, the fimbriated end is lined almost entirely with ciliated epithelium, while the secretory cells are abundant in the ampulla. At the isthmus, again, the secretory cells diminish in number, although they increase at certain phases of the cycle. Schaffer emphasizes the fact that in spite of the distribution of cells, the continuity of the ciliary action is never broken.

Schaffer is perhaps the chief proponent of the view that the secretory cells are not elements sui generis, but that they arise from modification of the ciliary cells. He supports this view by describing various transition phases. He discusses also the nature of the supposed secretion of the nonciliated cells. In some rodents, such as the rabbit, he believes that the cytoplasm granules suggest a mucinous character, and quotes Ellerman as having shown that in certain lower forms (amphibians) there are typical mucous cells between the ciliated ones. He agrees, however, that in most animals, including man, the nature of the secretion is not known. He does not believe that all the intercalary or ''peg'' cells are to be interpreted as emptied secretory cells. He calls attention to the fact that in some animals a primitive gland formation is to be seen in the fallopian tubes. Finally, he emphasizes the fact that the cilia are not by any means as perishable as many believe, and that they are easily demonstrable in fresh tissue for a considerable time after its removal from the body. The importance and ease of this method of study we shall emphasize in the report of our own work.

Hoehne (1908) studied the question of ciliation in both the uterus and tube. The former he found to show an interrupted ciliation, the latter to show a continuous ciliary stream. He was able to demonstrate cilia in the tube of a woman of sixty, who had passed through the menopause twelve years previously.

Holzbach (1908), in a comparative study of the cyclical changes in the lower animals and the human, suggests that the secretion may be of nutritional importance to the migrating egg. He believes that the muscle fibers of the tubal wall may assist in squeezing out this secretion. He found that ''Stiftchenzellen'' appear with the onset of estrus, and he discusses the various views which have been held as to their origin. Some of these have already been mentioned, but Holzbach calls attention to the observation made by Paneth that similar cells occur in other columnar epithelia, as in that of the small intestine, where they are to be interpreted as ''rests'' of goblet epithelium, which can again assume their customary form.

A second paper by Holzbach (1909) is devoted to a consideration of the question of tubal secretion. He demonstrated, by the Galeotti stain, that definite granules, presumably of the nature of a prosecretion, are to be seen in the cytoplasm of the secretory cells. The secretion is not mucin, and Holzbach again urges that it may be of importance to the nutrition of the egg. The secretory cells are increased at estrus and during pregnancy. This work was done with material from various rodents (rabbit, rat, mouse, hedgehog, bat).

Katz (1911), in the examination of five tubes in pregnancy, found the secretory cells much increased, and among them numerous cells which he considered transitions from the nonsecretory or ciliated type to the secretory.

Jägeroos (1912), in a study of 40 tubes from the premenstrual phase, gave an extremely accurate description of the two chief types of cells, as well as of their distribution. He discusses the view of Voinot, already mentioned, that at the time of menstruation there is a proliferation of the tubal epithelium, and quotes Delporte as observing that in the hypertrophied epithelium are to be seen

numerous "Stiftchenzellen," which are evidently only compressed epithelial cells. Jägeroos is inclined to agree with Schaffer as to the transformation of ciliated into secretory cells, and suggests that this transformation takes place at the time of menstruation, when the secretion is emptied and the cilia may be lost. This view is certainly incorrect, as will appear from our own studies, for the cells which possess the cilia before menstruation are not the ones which contain the secretion.

The excellent study of Moreaux (1913) is a model of painstaking and thorough histologic research. Like Schaffer, he believes that the secretory cells are derivatives of the ciliated cells, and he describes this transformation, step by step, with a precision that is most remarkable, although unfortunately it does not seem to have been corroborated by subsequent observers. The granules in the cytoplasm of the secretory cells he considers mucigenic in character. As the secretion collects, the cell bulges or herniates into the lumen, into which the secretion later is emptied. The later regeneration of the cell into a ciliated cell he ascribes chiefly to the influence of the "diplosome," represented by a pair of fine chromatin bodies, surrounded by a clear zone, and occupying different positions in the cytoplasm at different phases. Each diplosome divides and subdivides, giving an appearance like a row of diplococci, and this double row forms the basal granules of the new ciliated cell, the cilia developing from the outer row.

Moreaux divides the life cycle of the tubal epithelial cell into four phases: viz., (1) ciliation; (2) elaboration; (3) excretion; and (4) reconstruction. The stage of ciliation corresponds with estrus, i.e., with the presence of a mature follicle in the ovary. Excretion is noted after rupture of the follicles, when the corpus luteum has begun to develop, and when the ovum is going through the tube. Elaboration of secretion, therefore, he thinks is under the control of the follicle, while excretion is due to the influence of the corpus luteum. He suggests that the tubal secretion is probably of nutritional importance to the ovum, as will be discussed later.

Aschheim (1915), in his well-known study upon the glycogen content of uterine epithelium, mentions in an addendum that his pupil, McAllister, had been able to find glycogen in the tubal epithelium, although the study was still incomplete, and no relation had been demonstrated with the menstrual cycle. No later report on this work has been made, so far as we can learn.

Perhaps the most important study of recent years is that of Tröscher (1917), who studied 60 tubes in various phases of the cycle, as well as 2 fetal and 5 senile tubes. Secretory changes are not seen in the postmenstrual phase, during which the ciliated cells are predominant. In the interval, likewise, the mucosa of the ampulla particularly is lined almost entirely by ciliated cells. With the onset of the premenstrual period, however, the secretory cells are numerous and filled with secretion, and these changes persist if pregnancy supervenes.

Of his 60 tubes, 18 were from the interval phase, 15 from the premenstrual, 3 from the menstruating, 12 from the postmenstrual, while 12 were associated with pregnancy. All these tubal phases are quite adequately described. Tröscher's study is perhaps the most significant of any hitherto made from our present standpoint, inasmuch as it is perhaps the only one which has as its definite object the correlation of the tubal and endometrial cycle in the human.

The secretion, according to Tröscher, is not mucin, nor does he think that it is glycogen, although he occasionally found evidences of this substance. The "Stiftchenzellen" he believes are degeneration elements. Mitoses are rare, and are never seen in the ciliated cells. He quotes Geist, with whom he agrees, as to the nature of the changes in the tubal epithelium of the senile tubes. The folds become rounded, but the epithelium may be little changed for a considerable time, and

the basal granules may be clearly marked for a long period. Later the epithelium becomes cuboidal or perhaps almost flat.

Allen (1922) in a study of the estrus cycle in the mouse, described a characteristic extrusion of cell nuclei in the tubes during the early metoestrum, this being continued in marked degree sometimes to the middle of the following proestrum. This observation we consider of great importance from a comparative standpoint, as it would in this respect indicate a correspondence of the metoestrum in the lower animals with the premenstrual or menstrual phases in the human. On the other hand, during proestrus and estrus the nuclei of the outer third of the tube are arranged in a regular row, quite like that seen in the interval phase in the human. We shall discuss the significance of these facts later in this paper.

Snyder's studies (1923) upon the fallopian tubes of pigs demonstrated a definite cycle which closely paralleled the cycle of corpus luteum development. These cyclical changes involve not only the height of the epithelium, but also the surface and morphology of the nonciliated cells. The height of the epithelium was found to be more than twice as great when the ova are passing through the tubes (1 to 3 days after ovulation) as during the second week after ovulation, i.e., during the period of implantation. Snyder also describes the characteristic changes of the nonciliated cells after ovulation, changes which in the human being are noted in the premenstrual phase. This again emphasizes the very sharp difference in the chronology of the animal as compared with the human cycle.

In a second paper (1924) Snyder, working with human material, reported the results of his study of 75 tubes. Sixty-two of the tubes were from nonpregnant women at various phases of the cycle, and 13 were from pregnant women. He described very clearly the differences in height of the epithelium at various stages of the human cycle, with accurate measurements and beautiful illustrations. In 17 of the cases it was possible to study the endometrium also, giving opportunity for a correlation of the two cycles. Snyder's results, in the main, coincide with those of Tröscher, already referred to.

Scheyer's work (1926), on the lipoids of the tube, may be alluded to in passing, although its significance is not clear. He studied tubes from 7 patients. In the postmenstrual phase he found lipoid droplets in almost all the epithelial cells. In the premenstrual period, he also found lipoids abundant in the form of fine droplets, in both the epithelial and stromal cells. Lipoids are absent in the newborn, present in moderate amount during later childhood, abundant in 18.4 per cent of tubes during the reproductive era, and reach a maximum with increasing age, with its degenerative and atrophic changes.

Finally, a very recent paper in the Russian literature, by Jacovlev (1927) deals with the question of whether or not glycogen is to be found in the tubal epithelium. This author studied the tubes from 19 patients ranging from two days to fifty-five years of age. Five of these cases had extrauterine pregnancy. Glycogen was found in only 3 cases. One of these had a uterine pregnancy, the other two had extrauterine pregnancy. In the uterine gestation no glycogen was found in the epithelium, but only in the muscle and connective tissue. In the two cases of extrauterine pregnancy, he found tiny amounts of glycogen in the remains of decidual cells and in the folds at the point of rupture. No glycogen was found in the healthy part of the tube. In the main, therefore, it may be said that his studies as to the possible importance of glycogen in the tubal epithelium were quite negative.

MATERIAL UPON WHICH PRESENT STUDY IS BASED

The material upon which our own study is based consists of the tubes from 136 cases. In some cases both tubes were available, in

others only one. In addition to this fairly large series, a large number of other tubes were available for investigation, not being included in the series because of such reasons as inadequate data, pathologic changes, etc. The tubes included in the series were either perfectly normal, or else showed pathologic changes which were so slight as to have no bearing upon the cycle, as determined by comparison with the perfectly normal ones. Perhaps the majority of the tubes had been removed with myomatous uteri, while others had been associated with such conditions as uterine cancer, ovarian tumors, etc. The accompanying table indicates the distribution of our cases with reference to the various cyclic or other phases which were studied. The nomenclature of the various phases, viz., postmenstrual, interval, premenstrual, and menstruating, is the one commonly employed, being based upon the histologic picture presented by the endometrium, or upon an accurate menstrual history.

Of the 116 cases embraced under the combined heads of postmenstrual, interval, premenstrual, menstruating, and pregnant phases, it will be seen that in fully 105 we were fortunate in being able to study the endometrium as well. The importance of this fact is obvious, because of the fact that the endometrial picture constitutes a far more reliable indication of the menstrual phase than does the clinical history, for menstrual histories are notoriously prone to inaccuracies. Moreover, in a considerable number, there were available sections of the ovary, which, in some cases at least, furnish a further check upon the chronologic accuracy of the observations.

TABLE I

STAGE	NO. OF CASES	NO. OF CASES WITH ENDOMETRIUM	NO. OF CASES WITHOUT ENDOMETRIUM
Postmenstrual	17	15	2
Interval	62	54	8
Premenstrual	23	21	2
Menstruating	13	11	2
Pregnancy	4	3	1
Fetal	2	0	2
Senile	8	5	3
Hyperplasia with functional bleeding	7	7	0
Total	136	116	20

TYPES OF EPITHELIAL CELLS IN TUBAL MUCOSA

From a morphologic standpoint, three distinct types of cells may be described in the tubal epithelium, viz.: (1) ciliated; (2) nonciliated or "secretory"; (3) "peg" cells ("Stiftchenzellen"). While certain basic characteristics of these cells may be described in a general way, a study of any considerable number of tubes will at once impress one with the fact that they undergo striking variations at different phases

of the cycle, both as regards their individual morphology and also their distribution in the tube. These cyclical changes will be more fully discussed in the next section. The chief characteristics of these three types may be briefly summarized as follows:

1. *Ciliated Cells.*—These are most easily studied in the interval phase, when they reach their greatest development (Fig. 6). At this stage they are both tall and broad, measuring often as much as 30 to 35 microns in height, and as much as 12 microns in breadth. The cytoplasm is very pale staining and often almost refractile in appearance, although, by oil-immersion study, it will be found to show numerous fine granules, especially near the nucleus. The latter is quite large, and either round or, more often, slightly ovoid. Its long axis is not infrequently placed at right angles to the long axis of the cell. It is situated far above the basement
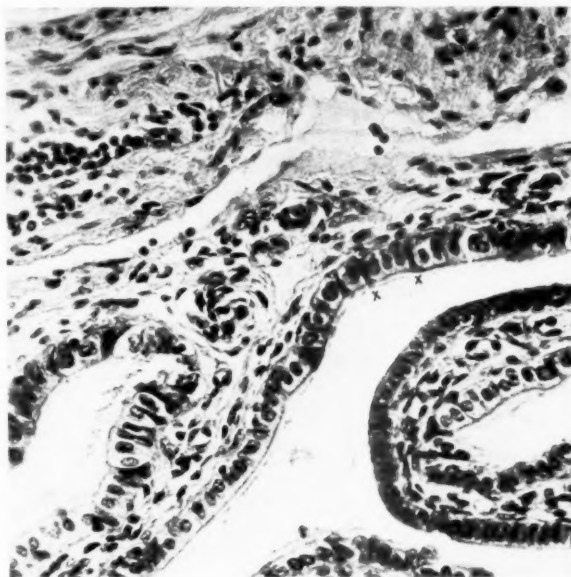
Fig. 1.—Tubal epithelium at end of menstruation, corresponding to endometrium shown in Fig. 2. The cells are low, the ciliated variety being still quite wide, and the nonciliated having given off their secretion, leaving only the nuclei. Most of the cells in the strip to the left are clearly ciliated, those on the right nonciliated. Note the dark rod-like "peg" cells at *x*.

membrane, often near the ciliated edge of the cell. This is in striking contrast with the nuclei of the nonciliated cells, which are much more deeply placed near the basement membrane (Fig. 6). This fact gives one, at first glance, the impression of a double layer of nuclei, the superficial belonging to the ciliated cells, the deeper to the nonciliated cells.

The differentiation of the two types is further facilitated by the difference in staining reaction, the nuclei of the ciliated cells taking rather a pale hematoxylon stain, as against the solid and darker stain of the nuclei of the nonciliated cells. The cilia are attached to a layer of basal granules, which, under proper magnification, stand out quite sharply. The cilia themselves, even in the fixed section, are quite long and slender, often measuring 7 or 8 microns in length. As many as a dozen or so are commonly to be seen in the ordinary section, with the high power. In many fixed sections, however, they show much clumping and agglutination, so that they cannot be readily recognized.

In the immediately postmenstrual phase the ciliated cells are much shorter than in the interval (Fig. 1), but they rather rapidly increase in height, as will be emphasized later (Fig. 3). Perhaps even more striking is the increase in breadth in the interval as compared with the postmenstrual phase. Beyond the interval, as we shall see, the ciliated cells again become low, and the minimum of height is seen in association with pregnancy (see below).

The simplest and most satisfactory manner of studying the cilia is in freshly removed unfixed tissue, primitive though this method may seem. It was, indeed by this method that the presence of cilia in the uterine epithelium of the sow was first demonstrated by Nylander as far back as 1851. The simple technic employed by this early investigator is still the best, and has been utilized by a number of subsequent workers. It consists simply in snipping off a tiny, thin bit of mucosa, placing it on a slide, flattening it out into a thin layer by pressure, and studying under the ordinary high dry lens. It is not necessary to add any physiological
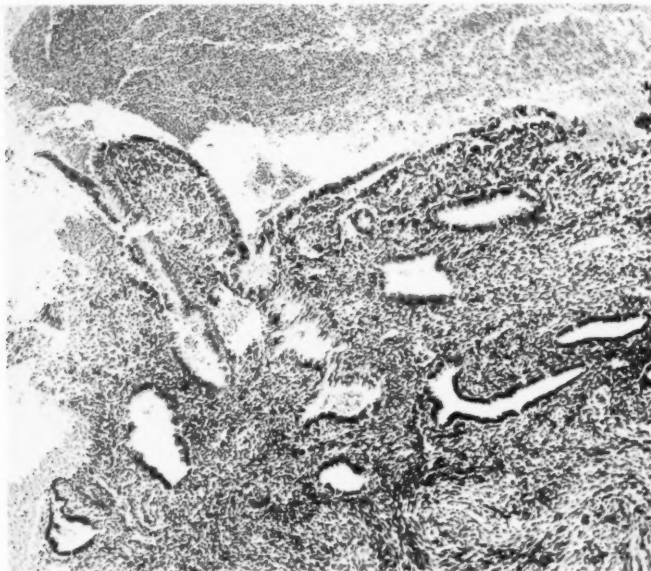
Fig. 2.—Endometrium from same case as that represented by tube in Fig. 1. This is the characteristic picture at the end of menstruation, showing the regeneration of the epithelial surface from the stumps of the uterine glands.

solution such as normal saline, Ringer's or Locke's. The cilia are of course best seen when part of the illumination is shut off. They retain their vitality for a surprisingly long time after removal of the tissue from the body, even when no effort is made to keep it warm. For the first hour or two their motility is vigorous, but we have noted definite ciliary activity for as long as four hours after the operation at which the tissue was removed.

The study of the cilia by this technic is a very fascinating one. To one who has not previously seen these cilia in action their vigor is apt to be most surprising. Even before the cilia themselves are discerned, one is often made sure of their presence by the considerable commotion which they create in their vicinity, especially among the red corpuscles which are commonly found in considerable number in sections prepared by the above technic. The cilia, too, appear much longer than in the fixed sections, at times seeming to be half the length of the cells themselves.

The cilia lash to and fro in surprisingly vigorous fashion, the direction of their propulsion being apparently always the same. One will often observe a red corpuscle being propelled along by this mechanism, the direct propulsion being assisted by the ciliary current of fluid which the beating of the cilia brings about. Whatever one's ideas may be as to the normal propulsion of the ovum the study of living cilia by this method will make it easy for him to believe that the cilia themselves, together with the ciliary current, are sufficient to explain the tubal transmigration of the egg, without the assistance of muscular peristalsis.

We have had the opportunity of studying the behavior of live cilia in tubes from all the phases of the cycle, as well as during pregnancy, and have not failed to find them under any of these conditions. This corresponds with our studies of fixed and stained tissues, for here likewise ciliated epithelium is to be seen at all these physiologic phases. Furthermore, as we shall see, they are
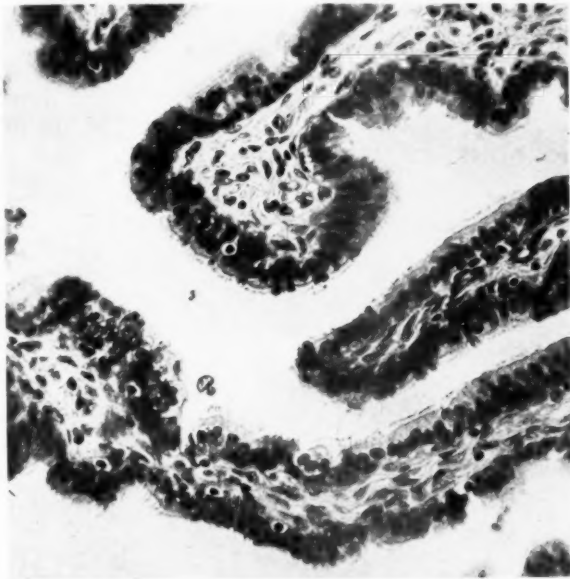
Fig. 3.—Tubal epithelium on sixth day of cycle, corresponding to endometrium shown in Fig. 4. The cells have already become quite high and narrow. There is no evidence of secretory activity. Cilia are well shown.

also found in the tubal epithelium long before puberty and long after the menopause. This suggests that they may have some function other than, or in addition to, that of assisting in the propulsion of the ova. Hartman (personal communication) suggests, with much plausibility, that their chief function may be merely that of keeping the tubal lumen cleansed of any foreign material.

2. *Nonciliated or "Secretory" Cells.*—These cells have been the object of even more extensive investigation than the ciliated cells, but as yet comparatively little is known as to their significance. From a morphologic standpoint, with which we are for the moment most concerned, there can be no doubt as to their essential difference from the ciliated elements. Like that of the ciliated cells, their height varies at different phases of the cycle. They are low immediately after menstruation (Fig. 1), become tall in the interval, remain tall in the premenstrual period (Fig. 8), and again become lower during menstruation (Fig. 12) and pregnancy (Fig. 14). In the postmenstrual period they are, like the ciliated cells, of narrow

cylindrical shape, so that at this time it requires a little sharper scrutiny to differentiate them from the latter. (Fig. 3.) The chief points of distinction, at this time, aside from the presence or absence of cilia (with proper allowance for absence due to imperfect preservation or preparation), are the shape, size, and staining of the nuclei, already described, the shape of the cell, and the staining of the cytoplasm. The latter is considerably darker and more uniform than with the ciliated cells.

In the interval phase the distinction between the two types is much more clearly marked (Fig. 6), partly by the increased width of the ciliated cells, their more easily recognized cilia, and the clear appearance of their cytoplasm, and partly by certain changes which now manifest themselves in the secretory cells. Whereas in an earlier phase these are narrow, almost rod-like in appearance, their free borders now become wider and perhaps slightly convex. There is thus produced an appearance suggesting a small cupola at the top of many of these cells, the cytoplasm
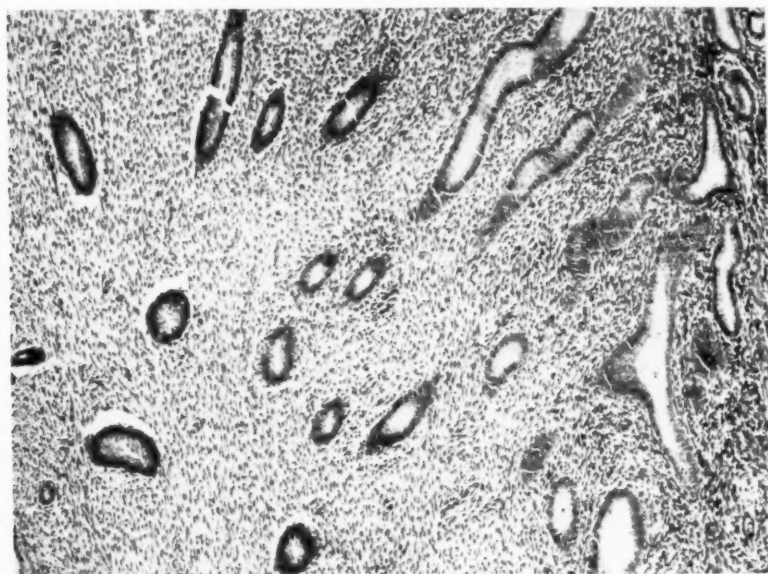
Fig. 4.—Endometrium from the same case as that shown in Fig. 3. A typical postmenstrual picture is seen with almost straight and very narrow glands.

appearing to herniate through the cell membrane, to use the term of Moreaux. The cell as a whole thus changes its shape, so that it becomes pear-shaped, or, perhaps from compression of its center by surrounding cells, dumb-bell shaped.

This variation in the shape and appearance of the nonciliated cells becomes more marked in the later stages of the interval. It is accentuated by the fact that, synchronously with this developmental phase shown by many cells, others exhibit changes which are apparently involutional or degenerative. The dome-like cell extremities appear to break into the tube lumen, leaving the nucleus with little or no discernible cytoplasmic envelope. Frequently too, the nucleus may be extruded into the lumen in a manner similar to that described by Allen in the tube of the mouse and by Hartman for the opossum. (Figs. 10 and 11.) This extrusion of nuclei is one of the most perplexing of all the phenomena. It can be taken as indicative of the death of the cell, but, extensive as the process often is, there is no evidence in the tubal epithelium of any regenerative activity. Mitoses are

almost never seen in the tubal epithelium, unlike the endometrium, where, during the postmenstrual phase, they are found in large numbers in both epithelium and stroma.

Another puzzling feature is the fact, already mentioned, that developmental and retrogressive changes proceed side by side, so that the reaction of the secretory cells to whatever the underlying stimulus may be appears to be to a considerable extent an individual one.   Certainly, however, it seems to be true that as the cycle advances toward the next menstrual period, there is an accumulation of cytoplasmic substance, commonly construed, on as yet very incomplete evidence, to be in the nature of a secretion.

With the advent of the premenstrual period itself, these changes become more pronounced, and another very striking feature is added.   Whereas up to this time the ciliated and nonciliated cells are of about the same height, there now appears
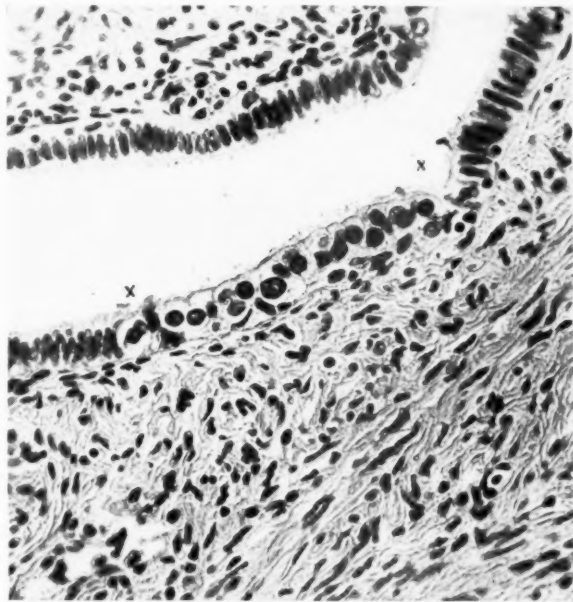
Fig. 5.—Tubal epithelium near the isthmus of the tube, showing the frequently patchy distribution of the two types of cells.   Most of the cells in the strip of epithelium between the points marked *x* are ciliated, while most of the remainder shown in this slide are nonciliated or secretory.   There is no evidence of secretion, as the tube was removed during the postmenstrual phase.

a marked disparity, so that the epithelial border becomes very irregular.   (Figs. 8 and 10.)   This is due less to an increase in the height of the nonciliated cells than to an actual diminution in the height of the ciliated elements.   The free borders of the former thus often project for a considerable distance above their ciliated neighbors, presenting a striking and characteristic picture.   (Fig. 8.)   The bulging ends of the "secretory" cells overhang the cilia, while extruded clumps of cytoplasm, often containing the cell nuclei, are to be seen, either matted to the cilia or else lying free in the lumen.

Nuclei are often seen lying quite naked on the free border, the cytoplasm having been emptied into the lumen.   Such nuclei are often wedge-shaped or triangular, being dove-tailed into the subjacent cells.   Often they retain a small amount of cytoplasm, suggesting that they retain a capacity for further cyclic change.

Still another factor which contributes to the premenstrual picture is the frequent occurrence of the ''secretory'' cells in clusters or tufts, not infrequently at the summits of the folds. Such clusters, sharply marked off from the adjoining ciliated cells, are made up of groups of from three or four to twelve or fifteen closely packed nuclei, with a varying amount of cytoplasm. (Fig. 8.) So closely placed are the nuclei that they often, at first glance, give the impression of a single giant nucleus. Sharp focusing, however, will reveal the outlines of the individual nuclei. This impression of crowding and compression is due partly to the increased development of the ''secretory'' cells, and partly to the elbowing of the ciliated cells, now much increased in width.

The changes in the secretory cells characterizing the premenstrual epoch are continued into the phase of actual menstruation, except that the cells become lower, and the cytoplasmic and nuclear extrusion is completed. At the end of menstruation
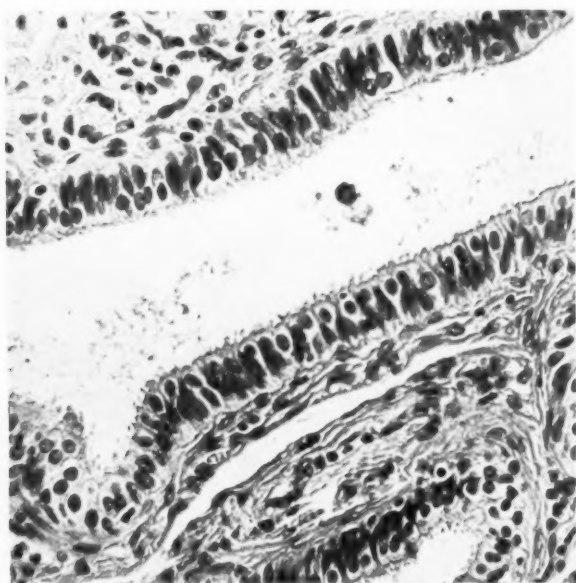
Fig. 6.—Tubal epithelium in the interval phase. Note the tallness of the epithelium, and the uniformity of the two types of cells, which are easily distinguishable in the picture. Note also the appearance of two rows of nuclei. The more superficial, rounded ones mark the ciliated cells; the darker ones, lying more deeply, mark the nonciliated cells. Cilia are seen in large numbers, but close examination shows that none of the secretory cells are ciliated. The endometrium of this case is shown in Fig. 7.

these cells appear to consist almost entirely of nucleus, although some of them show a moderate cytoplasmic envelope. (Fig. 1.) As with the ciliated cells, however, they soon become taller, assuming the slender cylindric outline already described as characterizing the postmenstrual period. (Fig. 3.) These cyclic changes will be further discussed later in this paper.

3. *Intercalary or ''Peg'' Cells (''Stiftchenzellen'' or ''Schaltzellen'').*—These cells are in many respects the least understood of the three types to be found in the tubal epithelium. Their characteristics can perhaps best be studied in the premenstrual and menstrual periods, when they are present in largest number. At these periods they present a rather striking appearance, being interjected at frequent intervals between groups of cells of the other two types. At first sight

they seem to consist of nothing but long, slender rod-like nuclei which are squeezed in between the adjoining cells. (Fig. 1.) It is for this reason that they may be spoken of as "peg cells," for they look not unlike slender pegs driven between the other cells. Throughout the literature they are rather commonly designated by the German term "Stiftchenzellen," or, by a few authors, as "Schaltzellen." The term "intercalary cells," employed by Voinot, would seem to be a very appropriate one.

While, with the ordinary hematoxylon-eosin stain, these cells most characteristically appear as intensely dark dashes between the neighboring cells, the nuclei not infrequently appear as wedge-like masses of nuclear material close to the basement membrane. By careful examination under the higher power, one will often discern a small amount of cytoplasm about the nucleus; sometimes most marked

Fig. 7.—Endometrium from the same case as that represented by Fig. 6. The picture is that of a rather late interval phase, with moderately tortuous glands, but no secretory activity of the epithelium.

at the base of the cell, sometimes near its free border, sometimes in both these regions. In the latter case the cell may be almost dumb-bell shaped. Under these conditions it cannot be distinguished from the "secretory" cell at a certain phase, as one will appreciate from the description already given of the latter cells. For example, in the menstruating tube, many of the "secretory" cells, emptied of their secretion, or, at any rate, deprived of the cytoplasm which has been thrown off into the tubal lumen, appear as peg cells.

For this reason, i.e., because we have been able to distinguish definite transition stages between these "peg" cells and the fully formed "secretory" cells, we believe that there is little doubt that the two represent different phases of the same life cycle. A number of other authors are inclined to the same view (Frommel, Mandl, Hörmann, Holzbach). If this conception is correct, it would indicate not only that the function of these cells is to form a cytoplasmic material which is

given off into the tube, but also that the cell, after this material is given off, still retains its vitality, and can perhaps repeat this process more or less indefinitely. This would perhaps explain the rarity of mitoses in the tubal epithelium.

This conception of the nature of the "Stiftchenzellen" is, however, by no means accepted by all authors, for a number of other theories have been suggested. Sobotta and Strahl, for example, suggested that these cells are only wandering leucocytes squeezing their way through the epithelium. This view is certainly incorrect, for morphologic if for no other reasons. It is true that migrating blood cells are often to be seen penetrating the epithelium, but their appearance is totally different from that presented by the cells under discussion. Reference has also been made to the view advanced by Bindi, a corollary to Sobotta's, to the effect that the intercalary cells, representing wandering blood cells, are concerned with the removal of degenerated spermatozoa from the tubal lumen.
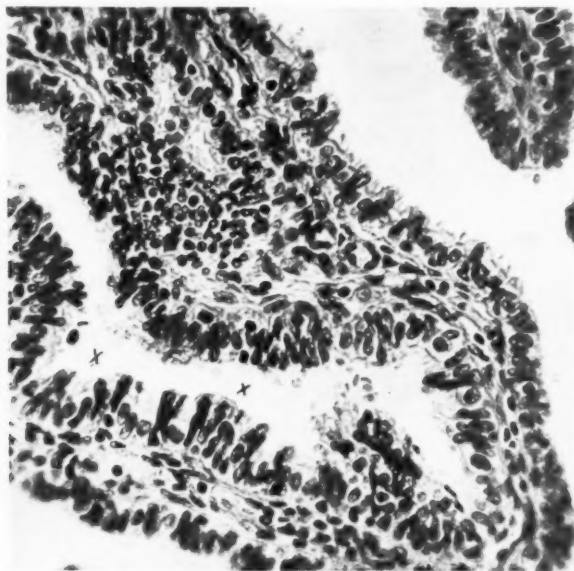
Fig. 8.—Tube in premenstrual phase, corresponding to endometrium shown in Fig. 9. The characteristic picture is especially well seen at x. Note the difference in height between the ciliated and the secretory cells, the nuclei of the latter protruding far above the margin of the now low ciliated cells. The cluster-like arrangement of the secretory cells is also seen. The irregularity of the border is often so marked that such tubes infrequently cannot be recognized at a glance even with the low power.

The interesting view advanced by von Ebner, to the effect that these cells are really of connective tissue rather than epithelial type, is one with which we were ourselves intrigued at first. Frequently these cells can be seen apparently arching or bending up into the epithelium from the underlying connective tissue stroma, and their nuclei are not unlike many of the long, narrow, and dark-staining nuclei of the connective tissue cells. Closer study, however, inclined us to believe that the suggestive pictures above mentioned were usually explained by the angle at which the particular epithelial strip had been cut. Furthermore, as we have already indicated, we were able to demonstrate intermediate stages between the "peg" cells and the fully formed secretory elements, so that we felt that there is no doubt of the epithelial nature of the former.

Schaffer does not believe that all of the "peg" cells represent emptied and compressed secretory cells, and agrees with the view that in part at least they represent

degenerated epithelial cells. Tröscher holds somewhat the same opinion. For this view, in the ordinary sense of the term "degeneration," we have found no evidence, unless one extends the term to the process of throwing off masses of cytoplasmic material. Reference has already been made to the view of Paneth, that these cells represent merely "rests" of secretory cells, analogous to similar rests of "goblet" epithelium, which he states occur in other columnar epithelia, such as that of the small intestine.

Finally, mention may be made of the contention of Kuhn that the intercalary cells are degeneration forms of the ciliated cells, a view which is not shared by any other investigator, and which our own material convinces us cannot be true. Throughout all phases of the cycle one must be impressed with the integrity maintained by the ciliated cells, aside from such unessential features as changes in height and width.
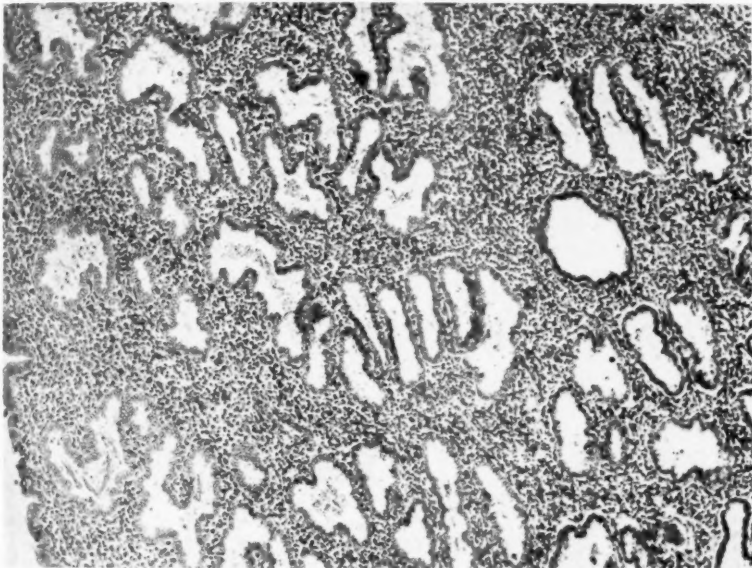
Fig. 9.—Typical premenstrual endometrium, with tortuous glands, secreting epithelium, etc. The tube from the same case as shown in Fig. 8.

CYCLIC CHANGES IN THE TUBAL EPITHELIUM

As stated early in this paper, the primary incentive for this study was to determine, if possible, whether a definite histologic cycle can be described in the tubal epithelium which is in any way comparable to that seen in the endometrium. While we have convinced ourselves that a cyclical variation does occur, it may be emphasized, at the outset, that it is not nearly so striking or so sharply definable as that in the endometrium. In the latter, the differentiation between the postmenstrual, interval, premenstrual and menstrual phases can be made at a glance, with a low power lens. The study of the tubal variations, on the other hand, is a much more laborious one, made only by rather tedious high-power study. Between certain phases, as be-

tween the interval and the premenstrual, the differentiation can often
be quickly and easily made. In other cases, on the other hand, the
distinction is made with much more difficulty.

The chief reason for this is the fact that the reaction of the tube at
different phases is not a uniform one, as in the case of the endo-
metrium. In the latter, the uterine mucosa everywhere in the normal
case presents pretty much the same picture. The reaction of the tube,
on the other hand, is a rather patchy one. For example, in tubes re-
moved shortly before menstruation, the premenstrual changes pre-
dominate, but in isolated areas the epithelium may still be very tall,
as in the interval. With regard to the secretory changes, the phases
are even less sharply marked off, as will be discussed later. In spite
of all these facts, however, nothing can be more certain than that the
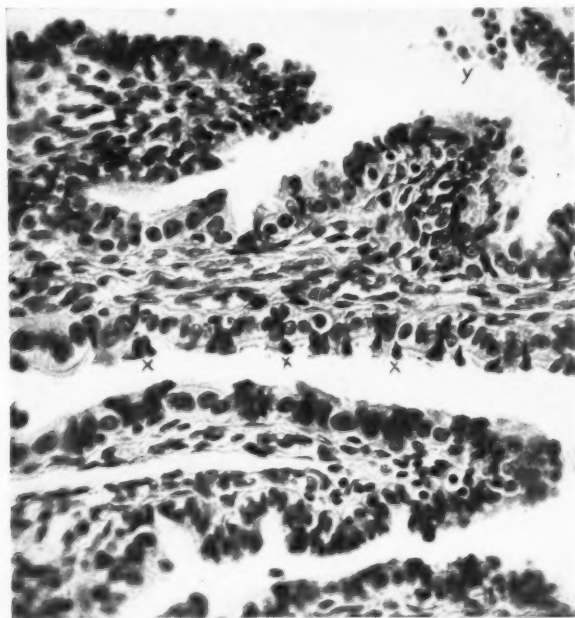
Fig. 10.—Premenstrual tube, showing (x) the peculiar extrusion of nuclei, which
is seen also in many of the lower animals (cf. Fig. 11). At Y is seen a collection
of such extruded nuclei lying free in the lumen, and quite similar to those seen in
Fig. 11.

tubal epithelium exhibits a cyclic histologic variation, so that careful
study will, with rare exceptions, enable one to determine at what
phase of the cycle it had been removed.

Although many of the cell characteristics at different phases have
already been discussed, we shall, in the following résumé, set forth
briefly our own observations as to the chief characteristics of the
tubal epithelium at the various phases of the cycle. The logical
method of presentation is under four heads, corresponding chrono-
logically with the four commonly described phases of the endome-

trium; viz., postmenstrual, interval, premenstrual, and menstrual. It
is not necessary to review here the characteristics of these endometrial
phases. Suffice it to say that the postmenstrual phase corresponds to
the first four or five days following menstruation, that this phase is
followed by the interval, which in turn continues up to five or six
days before menstruation. There is a tendency on the part of some
recent writers to place the beginning of the premenstrual or secretory
phase much earlier in the cycle, at the very first histologic manifesta-
tion of secretory activity in the endometrium, but this suggestion has
not been followed by us in this paper. The menstrual phase, of course,
represents the stage of actual menstrual bleeding. The distribution
of our cases is indicated in Table I.
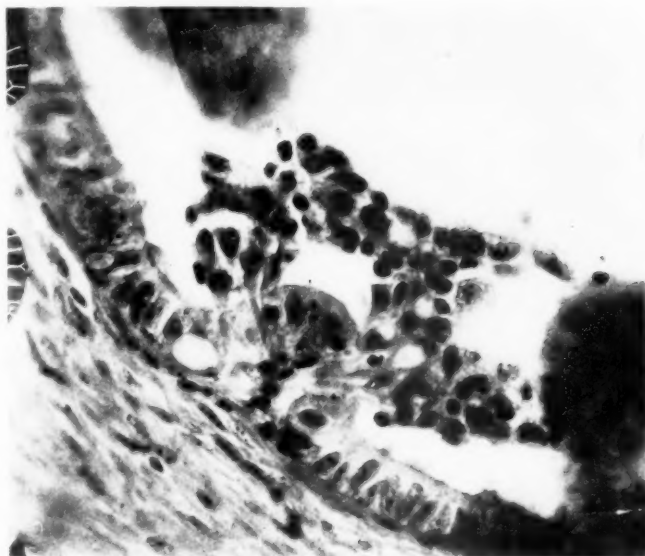
Fig. 11.—Tube of opossum 8 days after ovulation, showing clump of extruded nu-
clei in lumen, the process being the same as in the human (cf. Fig. 10). For this
picture I am indebted to Dr. Carl H. Hartman.

Postmenstrual Phase.—In the very early postmenstrual phase, immediately after
the cessation of menstruation, the tubal epithelium is still very low, measuring per-
haps only 10 to 15 microns in height. (Figs. 1 and 2.) The ciliated cells are still
broad and low, but the cilia are clearly discernible. The secretory cells have in part
become narrow and cylindrical, but many of them still show round or triangular
nuclei at the very border, left naked by the preceding stages. Rather rapidly the
height of both ciliated and nonciliated cells increases, so that, at the end of this
phase, they may be as much as 25 or even 30 microns in height. "Peg" cells are
seen only here and there. (Fig. 1.)

The cells are arranged in different proportions at different portions of the
tube wall. In many areas they are fairly evenly divided, although often their
distribution is patchy, i.e., short strips made up entirely of ciliated cells alternating
with short strips of the nonciliated type. This arrangement, it has seemed to
us, is more often seen at the isthmus than elsewhere. (Fig. 5.)

Interval Phase.—In this stage the appearance is quite characteristic, so that there is little possibility of mistaking it for any of the others. The chief characteristic, perhaps, is the great height of the cells (often 30 or 35 microns), their uniformity in this respect, the apparent increase of ciliated cells, their increased width, and the prominence of the cilia. (Figs. 6 and 7.) The secretory cells now show an increasing accumulation of cytoplasmic material, so that bud-like herniations of the free border, sometimes incorrectly interpreted as agglutinated cilia, are quite common.

An interesting observation may be noted at this point. In a considerable number of instances in which the endometrium showed a typical late interval picture, we have been surprised to find that the secretory cells in the tube had advanced to a stage of definite secretory change, similar to that which will presently be described as characterizing the premenstrual phase. In other words, the secretory phenomena
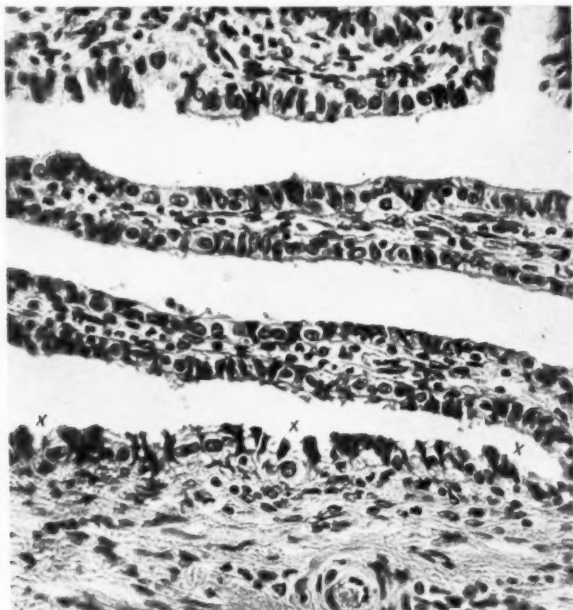
Fig. 12.—Tubal epithelium during menstruation (twenty-four hours after onset). The row of cells indicated at *x* shows persistence of premenstrual picture (cf. Figs. 8 and 10) while in other parts of the lumen the cells have assumed the more typical postmenstrual type, i.e., low and without secretion (cf. Fig. 1). The endometrium of this case is shown in Fig. 13.

appear to pass along the generative canal like a wave, striking the tube first and later passing down into the endometrium. The suggestion natural from this observation was that possibly these curious secretory phenomena were in some way linked up with the passage downward of the ovum, and, to proceed a step further, that perhaps the function of the secretion was to constitute either a protective envelope or a source of nutrition to the migrating ovum.

While this view is possibly correct, the chronology of the events in the sex cycle does not favor it. If the ovum is given off from the follicle at anywhere between the fifth and fifteenth day of the cycle, as most of us now believe, secretory changes in the tube, if of importance to the ovum, should manifest themselves much earlier in the cycle than they do. In other words, when this secretory activity in the tube

is at its height, the ovum has, presumably, long since passed beyond this point. This matter will be more fully discussed below.

Premenstrual Phase.—The characteristic premenstrual picture presented by the tubal epithelium can rarely be mistaken. The transition from the interval is not a sharp one, so that, in the early premenstrual period, the epithelium may still be of uniformly great height. Later, however, the epithelium becomes much lower, and especially the ciliated cells, which may now in many places be scarcely more than 15 microns in height. They are still broad and clear-staining, and the cilia are still conspicuous.

More interesting are the changes in the nonciliated cells, which proportionately are much taller than the ciliated, so that their free extremities project for a considerable distance above the latter. (Figs. 8 and 9.) Our study of human material indicates that this disproportion between the two types is rarely so extreme as that pictured by Snyder for the epithelium of the pig's tube, but it is sufficient to give
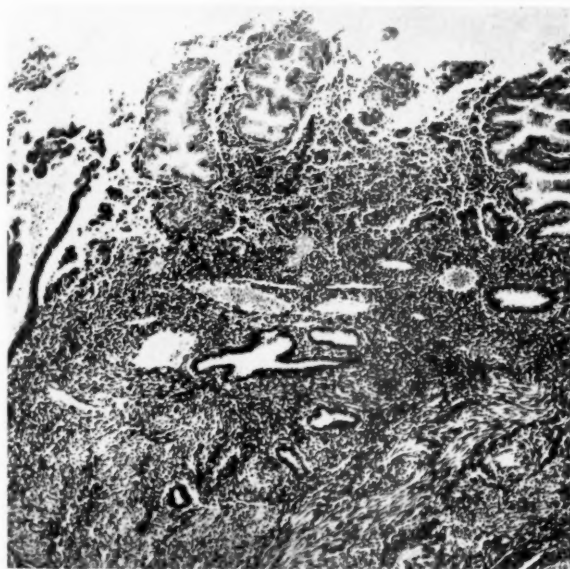
Fig. 13.—Endometrium from same case as the tube shown in Fig. 12.   The entire compacta, and most of the spongiosa, have been thrown off.

the free epithelial border a characteristically irregular or notched outline.   The projecting ends of the nonciliated cells are rounded or knob-like, because of an accumulation of cytoplasmic material. In many of the cells the process of extrusion of this material can be seen, and often collections of these cytoplasmic masses, resembling desquamated cells, can be seen in the lumen. Their real nature can be assumed from the fact that in many cells this process is caught, as it were, in actual operation. Not infrequently the nuclei are thrown off with the cytoplasmic masses, this constituting one of the most puzzling features of the whole process. (Figs. 10 and 11.)

In this stage, even more than in the preceding one, a curious cluster-like grouping of the secretory cells is seen, especially, though not exclusively, at the tops of the folds.   In these clusters may be seen from four or five to as many as twelve or fifteen of the characteristic dark, rod-like nuclei, spreading out in a fan-like manner from the basement membrane to the free epithelial border. (Fig. 8.)

The cells are so closely crowded together and often show so little cytoplasm that a first glance may give the impression of a large multinucleated cell. The nuclei often overlap so that, in many instances, only sharp focusing will show their distinctness.

Menstrual Phase.—With regard to this phase, the chief point of discussion, as stated early in this paper, has been the question of whether or not the tubal mucosa participates in the actual hemorrhage of menstruation. Many studies have been made on this point, the evidence now being quite conclusive that the normal tube plays no active part in the bleeding of menstruation. We shall not discuss this point in this paper, except to say that our studies of tubes removed during menstruation have convinced us that this now generally accepted view is correct. We have found no evidence whatsoever of actual menstrual bleeding from the tubal
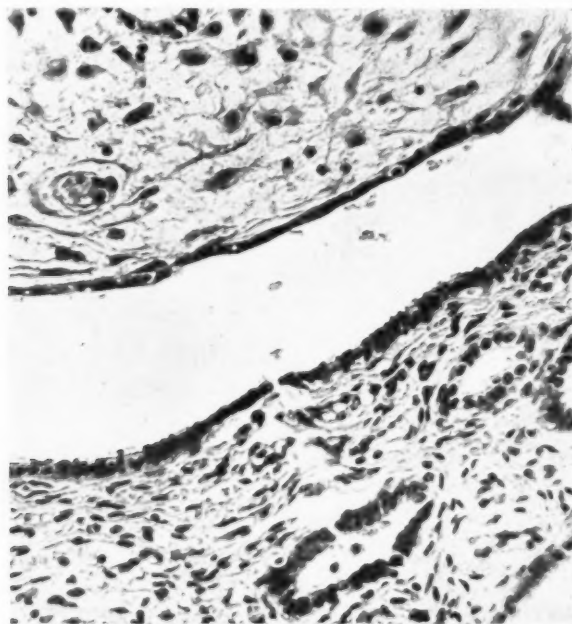
Fig. 14.—Tubal epithelium at about 4½ months' pregnancy (uterine). Above is seen a distinct decidual nodule in the tubal wall, a rather infrequent finding. Over it the epithelium is very flat, almost like simple squamous epithelium. This accords with the observation of Voinet (see historical review in text), although, as will be seen, the remainder of the tubal epithelium is also much lower than in the nonpregnant condition.

mucosa, although there is little doubt that the tube, like the other pelvic organs, participates in the general hyperemia which characterizes the menstrual phase, or, perhaps even more, the premenstrual epoch.

Examination of the tubal epithelium at the beginning of menstruation may show a picture essentially similar to that described for the premenstrual stage, except that the epithelium is somewhat lower. This feature becomes much more accentuated later in the process, so that, by the third day, the epithelial cells, of both types, are perhaps only 10 or 15 microns in height. As has already been emphasized, this change is not usually a uniform one, for in some parts of the tubal wall the

epithelium may still be quite high, perhaps as much as 25 microns in height. (Figs. 12 and 13.) The change, however, is always sufficiently extensive to be quite striking.

The ciliated cells are even lower than in the preceding stage, and still fairly broad, with clearly marked cilia. The secretory cells also become much shorter, chiefly from the loss of the large cytoplasmic bulbs so conspicuous in the premenstrual phase. The nuclei are thus left bare of cytoplasm, especially toward the lumen. This gives the epithelium a peculiar stubbly appearance which is rather characteristic.

"Peg" cells are still quite numerous. This is not surprising if one holds the view that they represent emptied secretory cells, or even if one considers them degenerated nonciliated cells.

Pregnancy Changes.—Only the changes of early pregnancy will be discussed, as the material of our laboratory has given us little opportunity to study those of late pregnancy. The pregnancy changes in the tube bear somewhat the same rela-
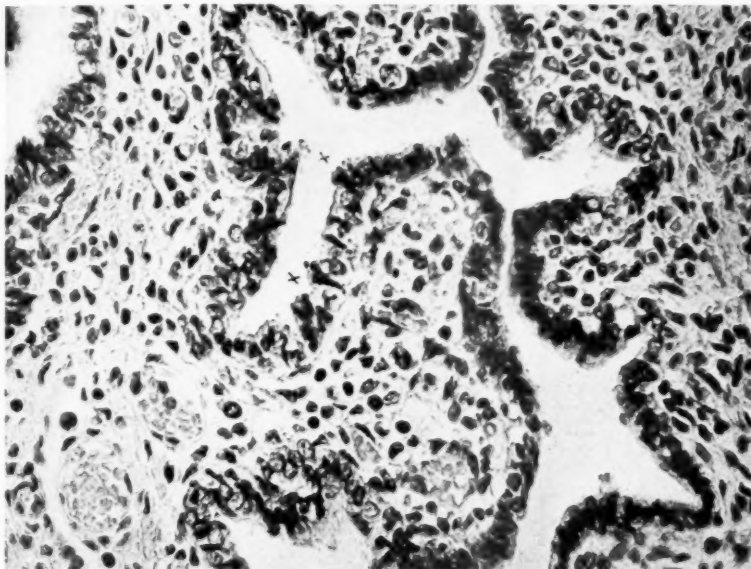
Fig. 15.—Epithelium of tube from infant born prematurely at 6 ½ months, and dying one month later. Both types of cells are clearly seen; especially at *x*. A few cilia are also seen, though imperfectly, in the same region.

tion to those of the premenstrual stage as do the changes of the corresponding phases in the endometrium, or in the corpus luteum. The tubal epithelium, low in the premenstrual period, becomes lower in case pregnancy supervenes. (Fig. 14.) The ciliated cells become extremely low, but still retain their cilia. The non-ciliated cells are also of short stature, of fairly regular outline, rather uniform size, and often show a slight convexity of the free border. Their appearance, however, is quite different from that of the premenstrual period, in which the cytoplasm appears to be actually bursting through the cell membrane into the lumen. In the gravid phase there is only a gentle rounding of the free end, often giving the epithelial border a finely wavy outline.

As further evidence of the similarity of reaction of the endometrium and endosalpinx to the pregnancy stimulus, we may add that, in cases of tubal pregnancy in which the death of the embryo has obviously occurred a considerable time

before operation, the tubal mucosa will no longer show the characteristics of the gravid phase, but will revert back to a quiescent postmenstrual or interval picture. This is equally true of the endometrium, which characteristically presents a similar quiescent picture, rather than that of decidua, in the usual cases of tubal pregnancy, where bleeding has been present for perhaps many weeks because of early destruction of the ovum.

RELATION BETWEEN THE CILIATED AND NONCILIATED CELLS

As will appear from the historic survey embodied in this paper, many authors have interested themselves in the possible relationship between the two chief types of cells.   A considerable number have
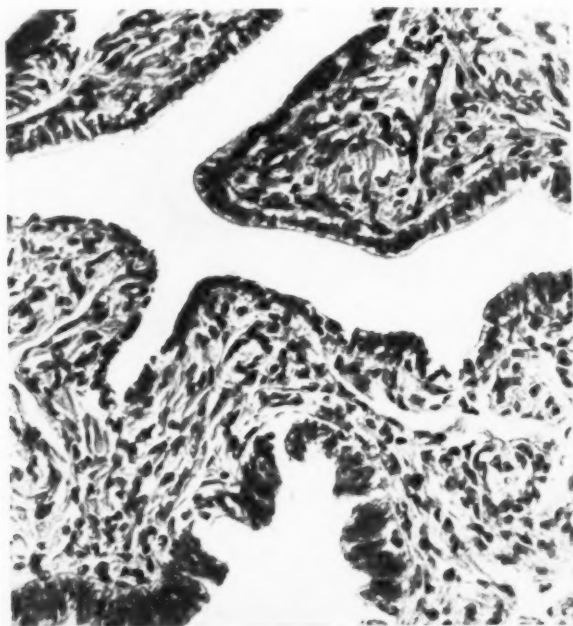
Fig. 16.—Tubal epithelium showing typical senile change.   The patient was sixty-three years old.   The epithelium at the lower part of the section is still remarkably tall, while that above has become quite flat, with a disappearance of cilia.   The latter, however, may persist for many years after the menopause.   Note also the rounding of the tubal folds.

supported the view that the secretory cells are merely modified ciliated cells (Nicolas, Voinot, Schaffer, etc.).   The chief ground for this belief is the demonstration of what have been interpreted as transition stages between the two types.   Our own feeling is that most of these supposed transition pictures are really only stages in the life history of the nonciliated cells, which are notoriously polymorphous.

It is difficult to see how a mere absence or apparent degeneration of cilia can be considered of much import as indicating a beginning transformation of ciliated into the nonciliated cell, when one con-

siders the frequency with which, in the ordinary fixed section, one notes these features in cells which, from a morphologic standpoint, are obviously of the ciliated type. If the studies of Moreaux upon the finer structure of the cells could be substantiated in the human, the evidence for this interchangeability of type would be quite convincing. So far as we know this has not yet been done.

Our own studies have led us to believe that there is some change in the proportion of the cells at different phases. For example, in the interval stage, the ciliated cells appear to outnumber the secretory, while the reverse appears to be true during the premenstrual phase. This variation, however, is rarely very striking, nor can it be con-
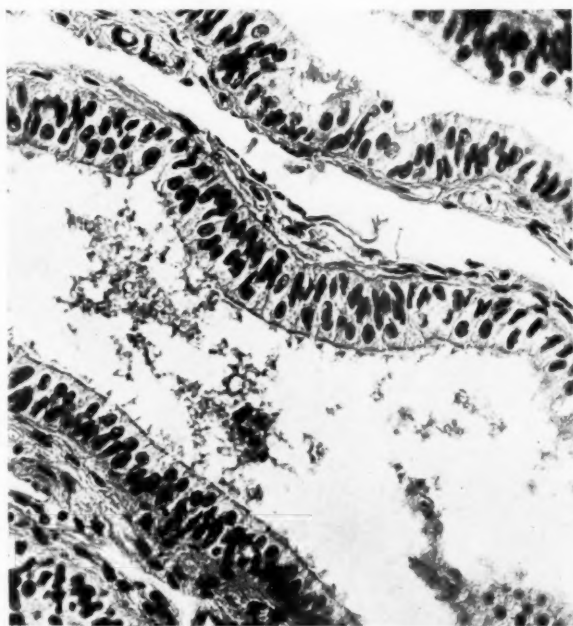
Fig. 17.—Tubal epithelium from a case of hyperplasia of the endometrium, with functional uterine bleeding. The ciliated cells predominate, and although the other type is seen, there is not the slightest sign of secretory activity. The epithelium is very tall, narrow, and compact. It appears to be a result of the persistence and continued growth of the interval mucosa, as would be expected from the etiology of the condition. The endometrium from this case is seen in Fig. 18.

sidered as evidence that one type is transformed into the other. Moreover, the indisputable fact remains that both types are found at all stages in fairly even proportion, and that this applies also to tubes before puberty and long after the menopause, when one can scarcely assume such a physiologic stimulus for cell variation as exists during the reproductive epoch. We are, therefore, inclined to the belief that the two types of cells are separate and distinct, although the problem must still be considered an unsettled one.

NATURE AND SIGNIFICANCE OF THE TUBAL "SECRETION"

This problem also has been discussed by a considerable number of those who have studied the tubal epithelium, although it is evident that the ideas expressed have, as a rule, been based upon speculative rather than scientific grounds. The views of a number of investigators on this point have been stated in the historical résumé which we have presented, so that they need not be again set forth (Mandl, Linari, Schaffer, Holzbach, Moreaux, Tröscher, etc.). Only an occasional writer, like Gurwitsch, appears to question that the nonciliated cells are actually secretory in function.
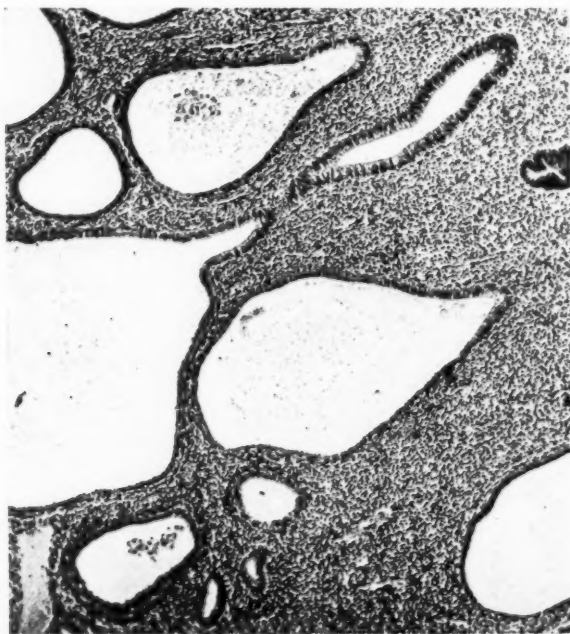
Fig. 18.—Typical hyperplasia of the endometrium, with the characteristic Swiss-cheese pattern of the glands. The patient suffered with functional menopausal bleeding. Compare with Fig. 17, which shows the tube from the same case.

And yet, when one analyzes the evidence, there is as yet no definite proof for such a function, except that of cell morphology, which is notoriously unreliable as an index of cell physiology. A number of investigators have attempted to study the question by differential staining methods, but the results have been practically negative. We ourselves have stained a considerable number of tubes with mucicarmin and thionin in an effort to demonstrate mucin, with negative results. We have also stained a considerable group with Best's stain, but have found no evidence of glycogen. Other workers (Tröscher, Jacovlev, Schaffer, etc.) have been equally unsuccessful.

This is in striking contrast with the demonstration in the premenstrual endometrium of both glycogen and mucin, with possibly a third substance of protein nature (Aschheim). This observation we have repeatedly confirmed. The uterine glands, therefore, are with much reason looked upon as the source of a secretion ("uterine milk") which is probably of importance to the ovum after it has reached the uterine cavity, and before it has implanted itself in the endometrium.

On teleologic grounds, the natural assumption would be that the tubal secretion, if it exists, is of importance to the ovum during its passage through the oviduct. We have, however, already referred to the fact that the height of the secretory activity is reached long after the ovum has passed through the tube, if the generally accepted views on this point are correct. On the other hand, it must be borne in mind that any secretion given off by the tubal epithelium would not long remain at the point of its discharge, for the vigorous propulsion of the cilia would carry it rapidly down the tube to the ovum, wherever it may be.

Here again attention may be called to the studies of Moreaux upon the rabbit's tube. This investigator found that if the egg is examined shortly after coitus, when still in the fimbriated end of the tube, it is bounded externally by the zona pellucida. If, however, the examination be made three days after coitus, when the ovum is near the uterus, it is found to be surrounded by a mucinous envelope which he designates as the "membrana zonale." That such a gelatinous capsule, whether protective or nutritional, actually exists in the rabbit we have been able to see for ourselves through the kindness of Dr. George L. Streeter, director of the Carnegie Institute of Embryology.

Schaffer likewise states that in rabbits and some other rodents the secretory cells show a coarsely granular prosecretion, which exhibits the characteristics of mucin. He quotes Ellermann as having demonstrated that in certain lower forms (amphibians) typical mucous cells are to be found scattered among the ciliated cells.

For such reasons as this there is much reason to believe that the nonciliated cells actually contribute a substance of some importance to the protection or nutrition of the ovum, in spite of the negative results which have thus far followed efforts to determine the nature of this substance. That cytoplasmic material in considerable amount is given off into the lumen cannot be doubted, and it would seem unbelievable that this process serves no useful purpose. The only other explanation one can think of is that the process is purely a degenerative one, and that it represents a cyclical cellular destruction perhaps comparable to the more massive and more easily demonstrable monthly desquamation of the endometrium.

With no evidence at all to bear on the point, it does not seem impossible to us that this peculiar cellular "secretion" of the tube, some

of which may readily enter the peritoneal cavity, may in some way be related with the etiology of endometriosis. There is much difference of opinion as to the correctness of the menstrual regurgitation theory of the causation of endometriosis, but the fact that the tubes are commonly patent lends much weight to the view that, whatever the cause may be, an important factor must be some substance derived from these open tubes. We are inclined to think that there is more plausibility in the view that the substance is derived from the tube itself than that it is regurgitated from the uterus.

The stimulus for the "secretory" activity of the nonciliated cells cannot be definitely stated. Like the corresponding phase in the uterine epithelium, the secretory stage in the endometrium begins just after ovulation, and advances synchronously with the development of the corpus luteum. It is probable, therefore, that the latter structure is responsible for this peculiar cell activity. Additional evidence for this belief lies in the fact that secretory changes in the tubal epithelium of such animals as the rat do not appear until the meteostrum, after the rupture of the follicle and the formation of the corpus luteum. Finally, as we shall stress in a later paragraph, the tubal epithelium associated with hyperplasia of the endometrium, in which condition corpora lutea are absent in the ovary, is characterized by an absence of secretory phenomena and a predominance of the ciliated cells.

The Tubal Epithelium in Early Life.—Being interested primarily in the cyclical changes in the adult tube, we have not studied the tubal epithelium in early life very intensively. On the basis of the few observations we have made, however, it may be said that the tubal epithelium of the newborn infant presents no very striking changes from that of the adult, other than an absence of cyclical change. The epithelial cells are somewhat lower, both the ciliated and the nonciliated. (Fig. 15.) The two types are clearly discernible, in spite of the fact that only a few of the cells which, from their morphology and distribution, are destined to become the ciliated cells, possess cilia at this period of life. This sparseness of cilia, according to Voinot, persists up to the time of puberty. In the tubal epithelium of a fetus of seven months we were able to find no cilia whatever, an observation which corresponds with that of Voinot on this point.

The Tubal Epithelium of Senility.—Perhaps the most surprising feature of the postmenopausal picture in the tubal epithelium is the fact that for a long time, perhaps several years, after the cessation of the menstrual cycle, there is little or no evidence of atrophic changes in the epithelium. The cells remain high, both types persisting, so that the picture is not unlike that seen in the interval phase of younger women. (Fig. 16.) The cilia are abundant, although there is no indication of

active secretory change in the nonciliated cells. In other words, the whole picture suggests that the growth stimulus due to the follicle hormone persists long after ovulation and corpus luteum formation have ceased. This, after all, is just what one would expect, for long after corpora lutea have disappeared from the ovaries, atretic follicles may be found in considerable number, presumably containing a certain amount of active follicle hormone, which exerts a growth-producing effect upon the tubal epithelium.

The persistence of cilia long after the menopause, like their appearance long before puberty, would indicate that they must have some function other than their supposed rôle in facilitating the passage of the ovum through the tube. This fact has already been discussed in a preceding paragraph.

Conspicuous atrophic changes are not seen except in the tubes of women of sixty or over. Cilia, for that matter, may be found even beyond this age. The tubal folds become more or less rounded, and the epithelium of cuboidal type, or even quite flattened. (Fig. 16.) As in other phases, these changes differ in degree in different parts of the tubal wall, so that in some parts of one section the epithelium may be fairly tall, in others quite flat, like simple squamous epithelium. In the flattened areas, of course, there is no trace of cilia, nor is it usually possible to distinguish the two chief types of cells.

The Tubal Epithelium in Cases of Hyperplasia of the Endometrium. —In view of the fact that hyperplasia of the endometrium, associated clinically with so-called functional uterine bleeding, is unquestionably due to a disturbance of the ovarian secretion, and that the endometrial response to this disturbance is a very characteristic one, it has seemed to us worth while studying the reaction to it of the segment of müllerian tissue comprised by the tube. Our material for this investigation is necessarily quite small, for it is only rarely nowadays that such cases come to abdominal operation.

The functional disorder in these cases is quite generally accepted as consisting of an absence of corpora lutea and an excess or persistence of the follicular stimulus. For details as to this point we may refer to the complete review of the subject by Novak and Martzloff in 1924. From what we have already said as to the physiologic response of the two chief types of tubal cells to the follicle and corpus luteum, one would expect to find, in cases of hyperplasia of the endometrium, a predominance of ciliated cells, with a subordination or absence of secretory activity on the part of the nonciliated cells. This is exactly what seems to occur, as will be evident from Fig. 17. The epithelium in general is tall and rather narrow, cilia are extremely abundant and well marked, while the nonciliated cells, though clearly differentiated, show no sign of secretory activity. (Figs. 17 and 18.) They often seem to show a genuine decrease in number, though this may be only

apparent because of the marked development of the ciliated cells. At any rate the picture is a very characteristic one. We have never in a case of hyperplasia of the endometrium seen any suggestion of marked secretory activity, nor do we believe that such a picture occurs in the tube, any more than it does in the endometrium.

SUMMARY

While the tubal mucosa does not participate in the bleeding of the menstrual process, its epithelium exhibits a definite cyclical change comparable with that of the endometrium. It is, however, not nearly so conspicuous as the latter, being concerned more with microscopic changes in the cells rather than with the grosser changes in pattern seen in the endometrium. The present study, based upon the careful examination of the tubes, from 136 cases, in almost all of which the endometrium was also available for study, has demonstrated the following chief facts:

1. The tubal epithelium consists of two chief types of cells, the ciliated and the nonciliated. The latter are often spoken of as "secretory" cells. A third type, the "peg" cells ("Stiftchenzellen," "Schaltzellen") are also described, but it is probable that these represent only a phase of the nonciliated cells.

2. In the interval phase, the epithelium is uniformly tall, the ciliated cells being broad, with rounded nuclei near the free margin, while the nonciliated cells are rather narrower, the nuclei being more deeply placed and taking a deeper stain.

3. In the premenstrual phase the ciliated cells become lower, so that the "secretory" cells project beyond them, giving the epithelial margin a ragged, uneven appearance. The "secretory" cells show a bulbous herniation into the lumen of the tube, often carrying the nucleus with it. This extrusion of nuclei is similar to that seen in many lower animals, but its significance is not known. In spite of the great loss of cells, mitoses are rarely seen in the tubal epithelium.

4. During the stage of menstruation, the premenstrual changes are carried further, the epithelium becoming quite low. The ciliated cells, especially, remain broad and low, but the secretory cells also, having been emptied of their cytoplasm, are much lessened in height, the nuclei often being quite bare of cytoplasm. "Peg" cells are numerous, their appearance and distribution suggesting that they are merely emptied "secretory" cells.

5. The postmenstrual phase is characterized first by a low epithelium, which quite rapidly, however, increases in height, so that by the third or fourth day after menstruation it is often almost as tall as during the interval phase. The cells are narrow, closely placed, and, after the first day or so, of uniform height.

6. During pregnancy, the epithelium becomes even lower than in the menstrual stage, and in the later stages it may become almost flat in many places. Secretory changes are not seen at this time.

7. Cilia can be demonstrated in all stages, especially through the examination of fresh tissues, by the technic described in the paper. They are also found in the tubal epithelium of young children and in women many years beyond the menopause. This suggests that they must have some other function than that of assisting in the propulsion of the ovum. Perhaps, as has been suggested by Hartman, their chief rôle may be that of keeping the tubal lumen cleansed of foreign particles of any kind.

8. Efforts at differential staining of the secretion have thus far been unsuccessful. Neither glycogen nor mucin can be demonstrated, unlike the findings in the secreting endometrium. The various views as to the significance of this tubal secretion are discussed in the paper, although there is as yet no positive knowledge as to this point.

9. The prepuberal tubal epithelium is rather low, but shows both chief types of cells. Cilia, however, are very sparse, and are usually not seen at all in fetal or very early postnatal life.

10. The epithelium of the postmenopausal tube may remain quite high for a surprisingly long time, perhaps a number of years after the cessation of menstruation. Cilia, likewise, may persist for many years. Sooner or later, however, the tubal folds become rounded, of fibrous appearance, the epithelium becomes low or even quite flat, and cilia, of course, disappear.

11. The tubal epithelium of tubes removed from patients suffering with hyperplasia of the endometrium was studied because the latter condition is unquestionably associated with a functional disturbance of the ovaries. Characteristically the epithelium was found to be high, uniform, compact, with narrow cells, most of which were ciliated. There was no evidence of secretory change. This bears out the view, for which there is other evidence, that the functional disturbance consists of an excess or persistence of the follicle stimulus, with an absence of the corpus luteum influence.

12. The comparison of the tubal cycle in women with that of the lower animals, like the comparative study of the uterine and ovarian cycles, emphasizes the important differences, chronologic and histologic, which exist. For example, the estrus tube of the rodent resembles, not the menstrual or premenstrual tube of the human, but the interval phase. Since estrus in the lower type is undoubtedly due to the follicle hormone, it seems clear that in the human the maximum of follicle influence is reached during the interval phase, and that the later changes are due to the corpus luteum influence.

To bear this out, the picture in the animal tube which resembles the human premenstrual tube is that seen in the metoestrum, during which stage the corpus luteum apparently plays the dominating rôle.

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26 E. PRESTON STREET.

GONOCOCCAL LESIONS OF THE FEMALE GENITALIA, INCLUDING CONSIDERATION OF SOME IMPORTANT CLOSELY ALLIED PROBLEMS*

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WORK in the laboratory has not added materially to my knowledge of pelvic infections since an address on this subject† one year ago. None the less, I am impelled to emphasize, in summary, certain views which have perhaps not aroused the interest which their importance merits.

I. PRINCIPLES UNDERLYING RECOVERY FROM INFECTIONS

Rest, drainage through natural channels and prevention of reinfection are the cardinal factors in the cure of all bacterial diseases not amenable to specific therapy. The value of excision of tissues for the purpose of eradication of infection has been greatly overstressed. Although sometimes essential, operation for removal of infection is too often resorted to as a routine procedure; correction of pathologic changes resultant from infection is a much more frequent indication for surgical intervention.

These statements are peculiarly applicable to gonococcal infections of the female genitalia.

II. PERSISTENCE OF GONOCOCCAL INFECTIONS OF THE LOWER GENITAL TRACT

Roughly expressed, gonococci tend to disappear from the tissues with a rapidity in inverse ratio to their distance from the vulva; external gonococcal infections are the most stubbornly persistent.

Whether infections of the urethra, Skene's ducts and the cervix persist because of anatomic peculiarities (including relatively poor drainage), or whether greater exposure to traumatism and to reinfection are responsible for the long-continued presence of gonococci in these tissues, is not yet a closed issue. Prolonged observation of an extensive series of women with unyielding infections has impressed me with the important rôle played by fresh reinfection in the maintenance of chronic gonorrhea of the urethra and of the cervix. Such evidence as is at present available indicates that every patient whose infection is resistant to treatment should be urged to avoid unprotected contact even though her sexual companion is apparently free from venereal disease.

Of all foci which harbor the gonococcus, infections in abscess pockets of Skene's ducts are perhaps the most persistent. The gonococcus also remains continuously viable in the deep urethral wall in those patients who have been subjected to intensive or traumatic treatments during the active course of the disease. Forceful treatments of the urethra, not only during the height of gonorrheal infection, but also during the descending wave of its activity, should be stamped with our unqualified disapproval.

Combined laboratory study and clinical experience formerly led me to the deduction that gonorrheal infections of the cervix are particu-
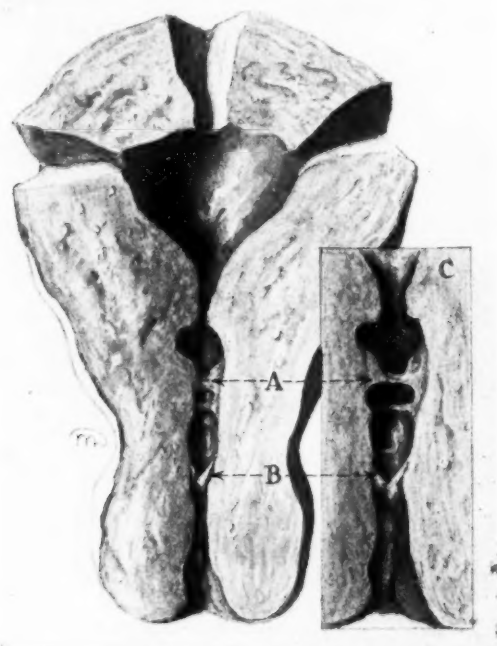
Fig. 1.—Cervical stricture. Patient aged fifty-four (menopause at forty-eight years). Purulent leucorrhea for one month prior to operation; no history of previous infection or instrumentation. A, Cicatricial bands with retention of purulent material above. B, Complete stricture impassable to dilator. C, Cervix spread open.

larly persistent. This belief appears to require some modification; consort reinfection accounts for more of these cases than was evident in my earlier experience, and gram-negative diplococci other than the gonococcus have gradually been found to occupy a somewhat more important rôle in the bacteriology of chronic cervicitis.

III. CERVICAL DRAINAGE

When we, as specialists, awaken to a full realization of the frequency and importance of cervical strictures, a great step forward will have been accomplished. Radium, the electric cautery, plastic

procedures upon the cervix, the Sturmdorf operation—even though resorted to with faultless technic—all contribute their quota of cervix obstructions. Office treatment for leucorrhea, dilation and curettage, gonococcal infections of the cervix whether treated or untreated, predispose to partial or complete stricture of the cervical canal in later years, notably after the menopause.

The otherwise inexplicable sudden appearance of leucorrhea after the climacterium is pathognomonic evidence of leakage of pent-up secretion through an unnatural cervical barrier. A case of this character is shown in the accompanying illustration (Fig. 1). This uterus was removed three weeks ago from a patient, aged fifty-four, six years after the menopause. Contrary to the usual rule there was no history of gonorrheal infection, abortion, local treatment, or operative manipulation.

Two other cases of complete stricture have been encountered within the last six weeks.

Obstructions of the cervical canal need not be complete; even though partial they are often sufficient to interfere materially with drainage. Sometimes the obstruction is friable, but relatively firm cicatrices are the rule. With the exception of the external os, the lower half of the cervical canal is less often involved.

Microscopic pockets in the wall of the endocervix may also be sufficient to prevent adequate drainage, even though there be no gross obstruction of the cervical canal. It is my experience that most patients with uncontrollable purulent leucorrhea of otherwise inexplicable etiology have lesions of this character. The electric cautery knife is particularly efficient in this type of case.

Emphasis of cervical strictures and microscopic endocervical pockets, which account for chronic leucorrhea through interference with drainage, is not intended to discount the importance of other causes of chronic leucorrhea. Easily demonstrable lacerations and repeated reinfections are outstanding factors in the etiology of intractable chronic cervicitis; pelvic congestion and specific parasitic infections also account for a considerable number of cases.

IV. "THICKENING" OF SKENE'S DUCTS; BARTHOLIN GLAND ENLARGEMENTS

Investigation of appropriately selected patients, subjected to correlated pelvic examination and painstaking study of their histories and the histories of their sexual companions, has convinced me that thickened Skene's ducts are pathognomonic of gonococcal infection. But we must recognize that many patients have "thick" ducts—thick by nature or acquired as a result of traumatism—which are rigid on palpation but are devoid of specific inflammatory reaction. There are many of these cases in which I find it impossible to deduce, without other evidence, whether Skene's ducts are "thick" or "thickened."

Enlarged Bartholin glands, in contrast with thickened Skene's ducts, are not always pathognomonic of gonococcal infection. Traumatism, injuries of childbirth and plastic operations account for many cases. *Bilateral* Bartholin gland enlargement is diagnostic of gonorrheal disease although, theoretically, injury might also involve both glands.

V. GONOCOCCAL INFECTIONS OF THE TUBES; INDICATIONS FOR OPERATION

Since 1921 we have almost discontinued operations for the purpose of eradication of tubal infections. In consequence I have little to add to my work on the bacteriology of relatively active tubal inflammations. Continued study of inactive tubal inflammations fails to reveal gonococci or "mixed" infections in cultures of thoroughly ground tubes; this experience is at variance with the belief of some authorities who assume that organisms associated with the gonococcus are frequently present and remain persistently viable. An occasional exception is a persistent tubo-ovarian abscess infection in patients free from suspicion of fresh reinfection; as a rule these are "mixed" infections.

In essential features further laboratory study and added clinical experience have confirmed earlier deductions: gonorrheal salpingitis is essentially a self-limited process; persistently active gonorrhea of the tubes is ascribable to recurrent infection rather than to chronic infection; with reinfection prevented the tubes heal spontaneously.

Eighty-five per cent of patients who come to us with acute salpingitis progress to a clinical cure without operation. Surgery is ultimately resorted to in approximately fifteen per cent of these cases, chiefly for relief from the sequelae of salpingitis; operations are directed to the reconstruction of tissues laid waste by disease rather than to removal of organs for the purpose of stamping out infection. The chief indications for intervention are:

1. Painful displacement of the uterus.
2. Adhesions with symptoms.
3. Uterine bleeding due to disturbed function of the ovaries.
4. Giant hydrosalpinx or tubo-ovarian cysts.
5. Rare cases of persistent tubo-ovarian abscess.
6. Unusual patients who, despite warning, repeatedly subject themselves to fresh tubal infection.
7. Selected sterility cases. Operation solely for relief of sterility is occasionally undertaken but is limited chiefly to those in whom the adnexa are not palpably enlarged.

VI. NOTES ON OPERATIVE TECHNIC

Widely accepted principles in operative technic merit casual mention: A portion of the body of the uterus should be removed at the time of salpingectomy if sterility is inevitable. Complete hysterectomy is indicated if the cervix is notably diseased. Suture of the ligaments into the uterine stump is not vitally important but is help-

ful if it can be done without producing undue tension or distortion. Removal of the appendix is perhaps best limited to those cases in which it is diseased or predisposed to future trouble. Routine gentle palpation of the contents of the entire abdominal cavity is advisable.

Disposition of ovaries at the time of operation; healed tubes encountered during hysterectomy.—As stated elsewhere, a decision relative to the disposition of a doubtful ovary requires most careful consideration of the etiology of the pelvic infection. If of gonorrheal origin, preservation of the ovaries appears desirable unless they are rather badly crippled or the circulation is impaired. If one ovary must be sacrificed it is inadvisable to resect a major portion of the remaining one; complete removal is preferable. Healthy prolapsed ovaries should be replaced into normal position. Operative displacement of the ovaries into the midline or suturing them to the uterine stump is objectionable. Sutures introduced into the ovarian substance invite trouble; cautery puncture of follicular cysts is also inadvisable because it predisposes to adhesions.

A healed tube which produces no symptoms does not necessarily require removal in patients subjected to hysterectomy; for three years we have made a practice of leaving undisturbed those smoothly healed tubes (including slight hydrosalpinx) which produce no symptoms and cannot be removed with the uterus without injury to the ovary or its circulation. My tendency is to spare an increasingly larger percentage of such tubes; this insures the function of the ovary and permits a simpler and neater pelvic toilet.

VII. QUESTIONS

In closing, I wish to present some queries for discussion at this time:

1. My experience indicates that, if one ovary must be sacrificed, resection of a major portion of the remaining one is frequently followed by interminable persistence of flushes and other menopause symptoms. In view of this evidence, are we justified in hoping for satisfactory results following transplantation of pieces of ovary?

2. Healed ovaries may be firmly imbedded in adhesions. In the absence of notable symptoms is it good surgery to leave such ovaries undisturbed at the time of operation?

3. Within two years at least three of my private patients have developed definite pelvic cellulitis subsequent to cautery treatment of the endocervix (fortunately all recovered relatively promptly). This complication is perhaps more common in those who have a retrodisplacement of the uterus. I have wondered whether others find that a single cautery knife treatment is always a harmless procedure.

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POSTPARTUM PELVIC INFECTIONS

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THE part assigned to me in this symposium is puerperal infection or infection occurring after full-time labor. It is obviously impossible to deal adequately with all parts of this subject in the time at my disposal and I shall, therefore, limit myself to a consideration of certain phases of the problem such as the source of the pathogenic organisms and their mode of entry to the genital tract in the parturient or puerperal woman, the mode of growth and dissemination of these organisms in such cases in contrast with their behavior in nonparturient cases and finally the end-results.

The more the subject of puerperal infection is studied the more complicated does it become. That sepsis has been practically eliminated from surgical practice and that its incidence in obstetric practice throughout the countries of the world has diminished so little has been held as a reproach to our profession. This reproach is deserved to the extent that it must be conceded that in the majority of cases in which septic infection occurs there has been some breach in technic or some error in judgment in the conduct of the case. In so far as this is true one must continue to teach that puerperal sepsis is a preventable disease. At the same time, without in any way trying to shirk our responsibilities as a profession or as individuals, it must be recognized that septic infection may occur in cases which have been handled with the greatest care and good judgment. I am led to dwell on this aspect of the subject because of the work done in recent years on the bacteriology of the genital tract, on the epidemiology of streptococcal diseases in general, and because of certain facts which emerged in a series of cases which occurred recently in the Sloane Hospital for Women, New York.

MODE OF ACCESS OF ORGANISMS TO GENITAL CANAL

It seems to have been proved beyond doubt that a considerable number of pregnant women harbor in their vaginas and cervices organisms which in their morphology and cultural characters are identical with those which under other circumstances cause infection. Of these the streptococci are the most important group. Dr. Jessie Eeles working in my Department in Edinburgh investigated a series of nonpregnant women and found that 45 per cent of these who had deficient pelvic floors and 20 per cent of nulliparae had streptococci

in the cervical canal. In seventy pregnant women only eight yielded sterile cultures from the cervix. In the others staphylococci, diphtheroid bacilli, and streptococci were found. In eleven of the cases, i.e., in 16 per cent, streptococci were present. These results are in general accord with those obtained by other investigators such as Fromme 16 per cent; Bumm and Sigwart 69 per cent; Doederlein 4 per cent; Walthard 27 per cent. Burt White and Armstrong assert that while various strains of streptococci including hemolytic varieties may be normal habitants of the vagina and cervix the streptococcus pyogenes is not. They state that "a hemolytic streptococcus is not necessarily identical with the streptococcus of puerperal sepsis unless proved virulent for laboratory animals." * * * "The significance of the presence of hemolytic streptococci in the cervical canal cannot be studied apart from the question of individual susceptibility." They show that while finding streptococci in the cervix of 35.9 per cent of pregnant women, in only one was the organism a true Streptococcus pyogenes. The patient in whom it was found had a normal puerperium.

There can be no doubt, therefore, that streptococci do occur in the vaginas of apparently healthy women. But the vast majority of these women escape any serious infection, from which we must conclude either that these organisms, even the hemolytic ones, are nonpathogenic or that the individual in whom they are found has become immunized against them. This possibility of a patient being immune to the organisms present in her vagina and the presumption that these are of the same type as those of her environment may account for the known fact that the dirtiest patient may be confined in her own home amid the most squalid surroundings with an entire absence of aseptic precaution and have a perfectly normal puerperium. Take her out of that environment and conduct the labor in the same casual way and she will, almost certainly, become septic.

But there is also the possibility that these organisms are potentially virulent and that given suitable conditions, such as bruised, lacerated, and devitalized tissues they may cause infection. There is the further possibility that even in the absence of the last named conditions, certain unknown cyclical changes inherent in the organisms themselves or determined by climatic, seasonal, and other environmental conditions may render them virulent. That members of the group of organisms known as streptococci have periodic waves of virulence is now a well-established fact, minor seasonal waves and major waves occurring in certain years. The accompanying graph, constructed by Mr. Norman P. Pleshette, one of our fourth year students, shows the seasonal incidence of deaths from puerperal sepsis during the past ten years in New York City. That outbreaks of puerperal sepsis are often coincident with an increased incidence of other streptococcal

infections has been frequently noted. (Watson, Dafoe.) This does not argue that these cases of puerperal sepsis occurring at such a time are necessarily or probably cases of autoinfection from vaginal streptococci. On the other hand Dr. Meleney came to the conclusion from the investigation of a streptococcal epidemic in the Sloane Hospital occurring at a time when other streptococcal infections were prevalent in the city that the type of organism was so constant in the different patients that it must have come from a common source and must have got into the genital canal immediately before, during, or after labor.
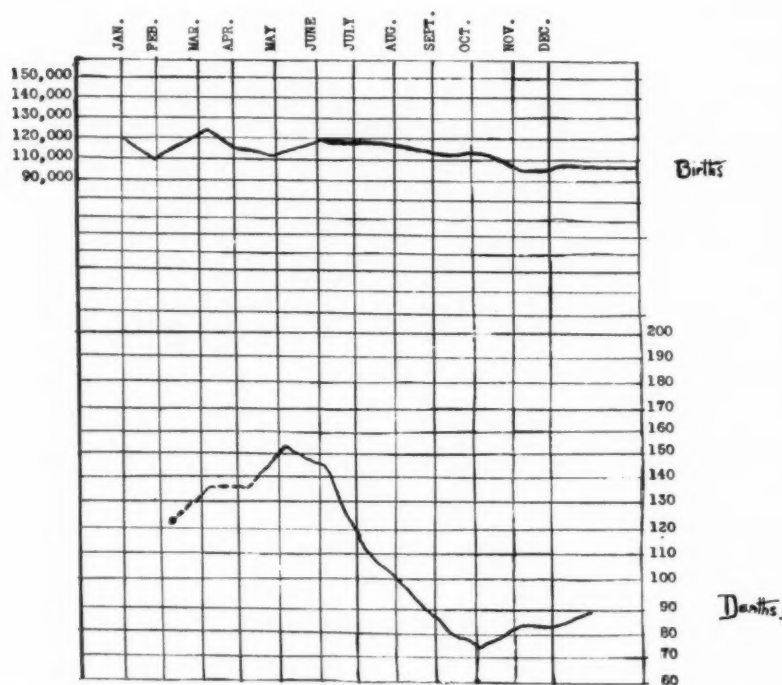
Fig. 1.—A comparison of the monthly birth rate with the corresponding death rate from puerperal sepsis, per 100,000 living and stillbirths, in New York City for the last ten years.

Not only do many women have streptococci and other organisms in the vagina and cervix prior to labor but practically every puerperal uterus contains organisms of various kinds by the third or fourth day of the puerperium (Natvig, Wegelius, Loeser). That the bacterial invasion may occur during labor has been shown by Harris and Browne who have demonstrated bacteria in the uterus in a large percentage of cases of cesarean sections performed more than four hours after the onset of labor. In some of these the membranes were unruptured and in some no vaginal examination had been made. It is thus evident that an absolutely aseptic field is impossible of attainment in

obstetrics and that the most we can hope to do is to prevent the entrance of alien organisms to the genital canal. The improvement in the morbidity rate reported by those who are using mercurocrome as a routine in the preparation of their patients may indicate that in it has been found an efficient agent for the destruction of both indigenous and alien organisms.

There seems to be no question that it is the alien and not the indigenous streptococcus which causes the vast majority of cases of serious puerperal infection. Its access to the genital canal may occur insidiously in cases where apparently every ordinary precaution has been observed. Attention will be called to one or two possibilities not yet generally recognized by the practitioner in the hope that if endorsed by this Society attention may be more generally called to them.

The first is the possibility of direct infection of the cervix and uterus from mismanagement of the third stage of labor. In cases where forcible attempts at expulsion of the placenta are made in such a way as to push the uterus down in the pelvis and make the cervix actually protrude at the vulva there is a grave danger of infection. On the release of the organ, material from the lower end of the vagina and vulva may be sucked up. The third stage is possibly the time above all others when infection is most likely to occur as it is a time when the tension on the operator is over and carelessness may easily creep in.

Then we must recognize the possibility of infection occurring in the early puerperium and one of the possible sources is the vulvar pad. Many of us have for this reason discarded the pad altogether, simply having the patient lie on a sterile square of aseptic absorbent covered with gauze.

With the carrying out of ordinary surgical cleansing of the hands and the use of sterile rubber gloves, there should be little risk of direct inoculation of organisms into wounds, but when worn for some time such gloves may become contaminated by fine spray from the nose or mouth of the operator. The nose and throat of healthy individuals in contact with cases of streptococcal infection very often contain the organisms. In our recent experience at Sloane Hospital, where we had twenty-five cases of streptococcal puerperal infection with nine deaths, the only situation in which we found the streptococci, other than in the infected patients, was in the nose and throat of certain members of the medical and nursing staff. Cultures from beds and bedding, pads, dressings, instruments, gloves, walls, floors, and air of wards and operating room were uniformly negative. We, therefore, came to the conclusion that the organism was being incubated in and disseminated from the noses and throats of these individuals. Hence, the importance of excluding all such carriers from contact with pa-

tients and of thorough masking of both mouth and nose by all in attendance on a woman in any stage of labor and in the early puerperium. A patient is probably more jeopardized by a carrier during and after the third stage than at any other time. In looking for and in repairing lacerations the operator is liable to infect his patient unless properly masked.

One other incident in the Sloane epidemic gives food for thought, viz., the occurrence of a generalized primary hemolytic streptococcal peritonitis in a nurse in attendance on one of the infected patients. The organism recovered from her peritoneal fluid was of the same type as that of the majority of our infected cases. How did that organism gain access? She had no sore throat, she had a negative throat culture, and no primary focus anywhere else could be found. And yet somehow that particular organism got into her peritoneal cavity.

Recently, many months after the epidemic referred to, a patient eight months pregnant was admitted to a private ward in the Sloane Hospital under the care of Dr. Damon with whom I saw her. She had all the symptoms and signs of a peritonitis. We did an immediate laparotomy and found a generalized peritonitis but no primary focus. A hemolytic staphylococcus was recovered from the peritoneal fluid. How did she become infected?

The pregnant and puerperal woman seems to be more susceptible to organismal infection than the nonpregnant and her resistance to infection when it is once established to be diminished. During the prevalence of streptococcal infections in the community she may apparently fall a victim to sepsis, the organisms entering her body by insidious ways and not necessarily by direct gross inoculation of the genital tract by those in attendance upon her. Until we know a great deal more of the life history, the methods of growth, the variations in virulence, and the portals of entry to the body of the bacteria of infection we shall be unable to prevent all cases of puerperal fever.

PATHOLOGY OF POSTPARTUM INFECTIONS

When infection does occur during or after labor a great variety of lesions may result. For the purpose of this symposium these can be only briefly reviewed in order to bring them into comparison and contrast with inflammatory lesions originating in other ways.

Owing to the great vascularity of the postpartum uterus, the large sinuses opening on the surface of the mucosa, the numerous and widely dilated lymph channels, and the rhythmic contractions of the uterine muscle, there is a greater tendency to wide dissemination of organisms by blood and lymph stream than in any other type of infection. If the organism, say a streptococcus, is a virulent one, it seldom stays long localized. By which channels—blood or lymph—it spreads

seems to depend to a certain extent upon the particular organism and upon whether the infection follows a full-time labor or an abortion. In a series of one hundred and sixty-three postmortem examinations in cases of postpartum and postabortum sepsis, Halban and Koehler found evidence of lymphatic spread in one hundred and fifteen and in forty-eight of these it was the sole method of dissemination. There seems to be a greater likelihood of direct blood stream invasion after abortion than after full-time labor. In five fatal cases of hemolytic streptococcal infection, all following full-time labor, recently investigated at the Sloane Hospital, autopsy showed in all of them a direct lymphatic spread through the uterine wall to the lymphatics in the cellular tissue and thence to the serous surfaces—pleura and peritoneum. In none was there any septic thrombophlebitis of the pelvic veins. In the majority of the cases with positive blood cultures the blood stream invasion occurred late in the disease, viz., on the second, fourth, eighth, tenth, eleventh, eighteenth, and twenty-sixth day postpartum. This together with the other evidences of lymphatic spread indicates that the organisms probably reached the blood through the thoracic duct. It is in cases of this type that the operation of drainage of the thoracic duct might do good.

In other series of cases there has been a greater incidence of direct blood stream infection, with or without septic thrombophlebitis, but in general it is fair to state that this is more common postabortum than postpartum.

Direct invasion of the peritoneal cavity through the lumina of the tubes is more frequent after abortion than after full-time labor, hence early peritonitis is commoner in the former than in the latter. Drainage of the peritoneum either through the abdominal wall or vaginal fornix is, therefore, more likely to be followed by good results in cases of peritonitis following abortion than in those following full-term labor where the peritonitis is so often a part of a general lymphatic and blood infection and really a terminal phenomenon. Peritonitis with loculated collections of pus throughout the cavity, often with abscesses in the ovary, is sometimes found in long drawn out cases of puerperal streptococcal infection and is practically always the result of a lymphatic spread. We had one such case in the Sloane epidemic of a year ago in which several of these abscesses were opened and drained but the patient ultimately died on the seventy-fifth day of her disease. At no time had she had a positive blood culture.

Localized Inflammation.—Fortunately the vast majority of puerperal infections do not become widely disseminated but there is this potentiality in all of them. More frequent and careful blood cultures have shown that organisms are present in the blood stream much more often than we formerly supposed and many believe that in every

intrauterine infection there is some escape of organisms into the blood. For this reason I am in agreement with those who would discard altogether the term "sapremia" as applied to puerperal uterine infections for I regard every case as a potential septicemia. In teaching I have found this view a great help in bringing home to the student the inadvisability of any interference with the interior of the septic uterus until we are reasonably sure that the activity of the organisms has ceased, as evidenced by a normal temperature for some days. From our experience of both active and conservative treatment most of us have no hesitation in preferring the latter. When so treated the majority of cases show no wide dissemination. In some the infection seems to remain localized to the interior of the uterus producing for some days a profuse, fetid lochia, tenderness, and delayed involution of the uterus and fever. Such patients make an apparently perfect recovery although as we shall discuss later there may be after effects in the form of chronic metritis and fibrosis uteri with its attendant symptoms.

In some of these cases where there is more or less localized tenderness over one or both sides of the fundus the question arises as to whether this is indicative of a salpingitis or of a cellulitis in the broad ligament. The latter is much more common than the former after full-time labor. The localization of the inflammatory process in the cellular tissue by lymphatic extension in a case of serious puerperal infection is something to rejoice in. It is very seldom that wide lymph or blood spread occurs in such. Careful watch on the size and character of the exudate and frequent leucocyte counts will reveal any pus formation and dissection along the cellular tissue planes. Early incision with drainage is called for under these circumstances. It is extraordinary how large these cellulitic exudates may become and how quickly and completely they absorb without the formation of pus and apparently without leaving behind any lesion within the peritoneal cavity. Such patients are less likely to suffer from late after effects such as chronic pelvic pain and sterility than those in whom there has been a postabortal infection. The following cases illustrate these points:

Mrs. R. developed a severe streptococcal infection beginning on the second day postpartum. Temperature was maintained at a high level for nineteen days and from the sixth day of her illness a mass was palpable in the pelvis and lower abdomen, which was diagnosed as a cellulitic exudate. Her temperature did not become normal until the fifty-second day and on discharge from hospital some thickening could still be felt on both sides of the uterus and around the cervix. Blood cultures throughout her illness were sterile. On her first visit to the Follow-Up Clinic two weeks after discharge the pelvis was found to be absolutely clear. This patient, fourteen months later, is five months pregnant and feeling perfectly well.

Mrs. C. had a severe hemolytic streptococcal infection beginning on the second day postpartum. Temperature intermittent and often reaching 105° F. up to the twentieth day. Blood culture negative. Marked swelling and induration developed in the pelvis all round the uterus. On the forty-first the exudate was explored and some pus evacuated. Patient was discharged from hospital on the fifty-seventh day when there was still considerable thickening and induration present but her temperature had been normal for a week. Four months later the mass had completely disappeared and there was only a little indefinite thickening to be felt. One month later she became pregnant. Her pregnancy was uneventful and she was delivered normally of a healthy seven and one-half months child followed by a normal puerperium. Examination of the pelvis one month after this showed no pelvic pathology.

Mrs. L. had a severe hemolytic streptococcal infection beginning on the second day postpartum. She had a temperature ranging between 104° and 100° F. for nineteen days. Blood culture negative. On the fifth day of her illness a tender mass could be palpated, to the left of the uterus, filling up the vaginal fornix. This mass had disappeared by the twenty-second day. Examination of the pelvis fourteen months later showed the uterus freely movable. No thickening to be felt. Cervix healthy with complete absence of catarrh.

Mrs. P. developed a severe hemolytic streptococcal infection on the third day of her puerperium. She was extremely ill. Very definite induration in both broad ligaments was detected on the tenth day of her illness. The inflammatory mass in the pelvis increased in size until the twenty-fifth day when it gradually began to decrease. On her discharge from the hospital on the fifty-first day it was still quite definite, most marked to the right, and in front of, the uterus. Two months later the mass had completely disappeared but slight thickening could be felt at the side of the cervix. Two months afterwards she became pregnant and had a normal pregnancy, labor, and puerperium.

For the following three histories I am indebted to Dr. W. E. Caldwell:

Mrs. S. was seen in consultation by the late Dr. W. E. Studdiford after attempted forceps delivery had failed. Her temperature was 104°, and Dr. Studdiford performed a craniotomy. Temperature continued high and a hard mass was palpated on the right side of the abdomen by the fourth day. On the sixth day there was a similar mass on the left side. These masses ultimately converged and when joined they reached above the umbilicus. On the twelfth day a double femoral phlebitis developed. Temperature reached normal at the end of six weeks and the mass began to diminish and had entirely disappeared six weeks later. Subsequently the cervix was amputated and the pelvic floor repaired. A year after this the patient became pregnant and was delivered by cesarean section at which time there was no evidence of any inflammatory disease in the pelvis.

Mrs. B. seen in consultation by Dr. W. E. Caldwell who performed craniotomy after her doctor had failed with forceps. Temperature at the time of delivery was 103° F. On the seventh day postpartum an indurated mass could be felt in the abdomen reaching up to the umbilicus. A week later a quantity of pus was evacuated through the posterior fornix. At the end of six months there was still considerable thickening to be felt in the pelvis. At the end of a year the uterus was found to be freely movable and in good position. Six months later she became pregnant. Cesarean section was performed at term. The only pathology found in the pelvis was marked varicosities in the broad ligaments.

Mrs. F. became severely infected after a craniotomy following failure to deliver by forceps by an outside practitioner. The temperature from the time of operation till six weeks later ranged from 100° to 104° F. On the fifth day induration could

be felt on both sides of the uterus. This extended until the inflammatory mass reached to the level of the umbilicus on both sides. By the end of three months these masses had disappeared and in another three months she was again pregnant. Cesarean section was performed at term and not a trace of adhesions or of inflammatory reaction could be found. Eighteen months later she had a second cesarean section.

These cases serve to illustrate the complete way in which inflammatory exudates following full-term labor may clear up and emphasize the wisdom of noninterference with pelvic inflammatory masses due to puerperal infections. I think we are all agreed on that, but the fact requires frequent repetition, for many lives are still being sacrificed through attempts at their extirpation. Even in those cases where the thickening persists and the patients suffer from chronic pain and disability we should hold our hand as long as possible. In some such there is tubal inflammation and peritonitis in addition to the parametritis. Curtis has shown that the streptococcus may remain potentially active for long periods of time in such tubes, and may cause serious and fatal reinfection when the tissues are contused and lacerated, as they always are, in dividing the dense adhesions present in such cases.

As has been mentioned, direct tubal infection with or without the subsequent formation of a pyosalpinx is less frequent after full-time labor than after abortion but it does occasionally occur. Most of these cases are gonococcal in origin. The old idea that the gonococcus may lie latent in the tubes during pregnancy, springing into activity after the first week of the puerperium has been discredited by the investigations of Curtis who failed to find gonococci in any tube after ten days of normal temperature. We must, therefore, come to the conclusion that when a gonococcal pus tube does develop in the puerperium it must be by an ascent of the organisms from the lower genital passages in the early puerperium. Hence the necessity for active treatment during pregnancy. The treatment of such cases as do develop pyosalpinx should follow the general lines of conservatism practiced in the nonpuerperal woman.

The indications for active surgical treatment in puerperal infections are few in number. Occasionally a definite abscess develops in the uterine wall as the result of a lymphatic spread and, in such, hysterectomy is called for. The diagnosis of such cases can only be made after some time has elapsed and the uterus is found to be definitely enlarged, irregular in outline, and tender. Such findings are compatible with the presence of a degenerating fibroid and the differential diagnosis may be difficult or impossible till the abdomen is opened.

Much has been written regarding the surgical treatment of septic pelvic thrombophlebitis and some brilliant results have been recorded. In 1917 Jeff Miller computed the mortality in the cases recorded in

the literature as 32.9 per cent. Baldwin advocates the complete extirpation of the uterus along with the thrombosed veins without ligation and with free drainage per vaginam. From this procedure he had a mortality of 29.8 per cent. Operative treatment is certainly advisable in some cases but the difficulty is in making a correct diagnosis. This cannot be done until symptoms have been present for a considerable time. The persistence of the characteristic swinging temperature, with frequent rigors and the detection in the pelvis of a more or less definite thickening on one or both sides of the uterus, should make diagnosis probable. In determining for or against operation in such a case, it is necessary to take frequent blood cultures. If organisms cannot be cultivated, or are only present at the time of the rigors and not in the intervals, the case is favorable. In such there is no true septicemia. There is merely a flooding of the blood with organisms from time to time, and then they are killed off in the blood stream. If a positive culture can be obtained at all times a general septicemia is present, and the outcome of operation is not likely to be good. In the great majority of cases there is some cellulitic involvement in the neighborhood of the veins, and the more rational procedure would seem to be that carried out by Baldwin and others of cutting across and removing the veins, and, if necessary, the uterus, and draining the pelvis rather than mere ligation.

Operation must not be postponed too long, but, on the other hand, many cases of puerperal sepsis which recover must have septic thrombosis in the pelvic veins. It is seldom that a sufficiently definite diagnosis, to justify operation, can be made before a fortnight or three weeks after the initial infection, and, in many cases, it will be longer. I have had no personal experience of the operation. In one case with characteristic symptoms I had all preparations for operation made on two separate occasions, but each time put it off. After running a very hectic temperature, with rigors often twice daily for seven weeks, that patient ultimately recovered.

While it is thus true that in the majority of serious cases of puerperal infection which survive, recovery is complete and there are few after effects, it may be otherwise with some of the less severe cases.

We have still much to learn regarding the subacute and chronic infections of the cervix and uterus initiated at childbirth and in the puerperium. What are the organisms principally responsible for these cases of endocervicitis of which we see so many? Are they indigenous bacteria of the vagina or are they introduced from without? Can we by paying more attention to the cervix in the early and late puerperium prevent their growth and action?

I was much impressed by a paper which Dr. Goodall read at a recent meeting of the New York Obstetrical Society in which he stated that inflammatory lesions of the cervix, many of them due to a strepto-

coccus, were demonstrable at an early stage of the puerperium. How many of us on the discharge of our patients from hospital make a thorough specular examination of the cervix and when lesions are found at once institute treatment? I confess myself a sinner in this respect and there may be others. Here is a big field of preventive medicine right at our hand.

Is there not an inflammatory etiology behind many of the cases of chronic metritis and fibrosis uteri with their attendant menorrhagias? Histologic examination does not always give definite evidence of it but the feeling of well-being and the improvement of health in these patients after hysterectomy has always seemed to me to be out of proportion to what might be expected from the mere stopping of the excessive bleeding. It is as if some definite focus of septic absorption had been removed. A similar rapid improvement in general health does not in my experience follow radium or x-ray treatment.

In this necessarily incomplete consideration of the subject of post-partum pelvic infections I have been able to touch on only a few points, leaving to those who will follow in the discussion the filling in of the gaps.

To focus that discussion the following broad generalizations may be stated:

1. The majority of severe puerperal inflammatory lesions are due to infection by organisms introduced from without.

2. The portal of entry of these organisms may not always be the external genital canal.

3. Indigenous vaginal and cervical organisms may cause serious pelvic inflammation and also less severe and more chronic lesions of cervix and uterus.

4. Localized puerperal inflammatory exudates tend to absorb and usually do so completely, leaving no after effects.

5. In serious infections conservative rather than radical treatment gives the best results.

6. In the less severe infections of the cervix and uterus more accurate diagnosis and earlier treatment might prevent later trouble.

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THE TREATMENT OF SEPTIC ABORTION

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THE problem of abortion has become world-wide. A steady increase in its frequency had been noticed in all countries for the past thirty years or more, but in the last decade this increase has been positively appalling. In 1890, there was, in Germany, one abortion to every ten births;[1] in 1911, the proportion had dropped to 1:5.[2] In 1919, in Hamburg, to quote but one example, one abortion occurred for every two births;[3] and in 1926, there were in the same city two abortions for every three births.[4] The actual number of abortions each year in Germany is somewhere between 500,000[2] and 875,750.[5]

Conditions in this country are, probably, not quite so bad though for lack of any statistics we may not be too sure about it.

This enormous increase is brought about almost altogether by criminal interruption of pregnancy whether carried out by shady physicians or midwives, by persons without any sort of previous training, or by the patients themselves. Compared with this, all other etiologic factors of abortion sink into insignificance. Ninety per cent[2] or more[5] of all abortions are criminal abortions.

A large number of such abortions becomes febrile, that is, results in infection. In 1917, the percentage of septic abortions was estimated at about 10;[6] today it is, probably, much higher. Death from infection occurs in so great a proportion that the mortality of criminal abortion far exceeds that of childbirth in general;[5] while the morbidity with its far-reaching influence upon the later life and health of the individual remains wholly incalculable.

There is, therefore, every reason to search for the most efficient treatment of criminal abortion, since we as physicians cannot hope to prevent the widespread evil by influencing its underlying social, economic and moral causes.

Treatment of criminal abortion is synonymous with that of septic abortion; for, owing to its clandestine nature, we hardly ever are called upon to treat a case of this kind until complications have set in. Such a patient, as a rule, has been bleeding more or less profusely for some time and, consequently, is in a state of secondary anemia. There is usually an ill-smelling vaginal discharge. Fever, varying in degree, is present and is particularly ominous if the pulse rate is too high in proportion. Chills and pain denote complications outside of the uterus, such as parametritis, pyosalpinx, pelvic peritonitis, throm-

bophlebitis, and general peritonitis; and there is always the possibility that the abortionist may have produced a perforating traumatism in some part of the genital tract.

I am fully aware that a febrile incomplete abortion may occur spontaneously either by ascent of bacteria from the vagina or cervix or by way of the blood stream in acute infectious diseases, but I think it is a good practical rule to consider every such case a criminal abortion until the contrary has been proved.

This attitude must needs influence our therapeutic actions and assist us in selecting from the multitude of remedial measures which have been recommended. This very multitude is, of course, a disheartening indication of the fact that our treatment of septic abortion is far from satisfactory.

We may divide the therapy into general or systemic, and local treatment.

As to general treatment, three methods have been suggested.

Specific therapy by means of vaccines and serums, despite its generally disappointing results, still has its advocates.[7]

Chemotherapy, that is, the introduction of antiseptic solutions into the circulation, has always been unsuccessful and often enough disastrous in its effects. Nevertheless it is being revived at present in the intravenous injection of mercurochrome though the necropsy findings studied in the chief medical examiner's department of the city of New York[8] leave no doubt as to the high toxicity of mercurochrome whereby lesions in kidneys and intestines are produced which may contribute to death.

Moreover, it seems an elusive hope in any blood-stream infection to kill all bacteria circulating in the blood by injecting a bactericidal solution into the vein. If there are no bacteria, but only their toxins in the blood, it is even more difficult to see how any such treatment can be of benefit. At any rate, any antiseptic solution strong enough to kill bacteria, will also do damage to the blood cells, the walls of the blood vessels, and the surrounding tissues.

Much better founded theoretically and far superior in its practical results than either of the two methods, is the nonspecific protein therapy by which the natural power, of resistance against infection is raised and the means of self-defense of the body are stimulated to most intense activity. Therein lies at once its strength and its limitation. For it is obvious that hopelessly damaged or worn-out cells cannot be revived by any stimulus however powerful. The percentage of failures, therefore, will be proportionate to the stage and intensity of the infection when it is first encountered. The relative harmlessness of protein injections, however, justifies a trial even in severe infections. Whether the protein therapy takes the form of intramuscular injections of milk, as advocated by me before this society four

years ago[9] or of repeated blood transfusions, as recommended by Polak,[10] is, to my mind, of less importance than the promptness with which this treatment is instituted, and its employment in conjunction with other measures known to act as cell stimuli, such as fresh air, sunshine, strengthening food, etc.

Hofbauer[11] adds pituitary extract, administered intravenously, to protein injections, and Küstner[12] recommends strong alcoholic drinks in large doses, both with the view of stimulating the heart.

The local treatment of septic abortion revolves about the question : Should the aborting uterus be emptied in the presence of fever? Here again we find three main procedures, namely :

1. *Active Treatment.*—In every febrile abortion the uterus is cleaned out immediately unless there are inflammatory complications in the vicinity of the uterus. Whether the evacuation should be done by digital or instrumental curettage is still a moot point.

2. *Expectant Treatment.*—Place the patient under a generally strengthening régime and wait for the fever to subside. From three to eight or more days later evacuate the uterus if the latter has not emptied itself spontaneously by that time.

3. *Conservative Treatment.*—No local manipulations are permitted, and the expulsion of the uterine contents is brought about solely by quinine, pituitrin, and the like.

The advocates of both the expectant and conservative treatments consider immediate evacuation indicated only if a dangerous hemorrhage occurs. This, however, is very rare.

We cannot pass lightly over any of these conflicting views because each of them is represented by men of recognized ability, experience, and judgment. The most natural thing would be to adopt that method which statistically has yielded the best results. Unfortunately, the problem cannot be solved in this way. Heynemann[2] has shown very convincingly the many sources of error which in this particular question render statistics unreliable. Moreover, if one studies the figures presented in the literature, the actual differences in the end-results from one or the other form of treatment are much too slight to permit of definite conclusions.

The advocates of active treatment claim that in daily practice the hand of the physician is forced by the demand on the part of the patient or her family for immediate relief. Any temporizing will drive the patient to another physician. An abortion, they say, terminates only when the uterus is empty. Bleeding ceases then at once, and fever, perhaps with the exception of a solitary chill after curettage, disappears promptly. Convalescence is, therefore, shortened ; the reduced duration of hospitalization and earlier return to work lessen the economic hardship.

Such a favorable outcome, however, is not always the rule. Curettage is often followed by a serious aggravation of the infection. The protective wall of leucocytes and fibrin is broken through, and the organism may be flooded by bacteria or their toxins. Hence, a superficial and not dangerous infection might conceivably be converted into one with strongly invasive qualities.[14] Parametric or perimetritic inflammation may then be the consequence, and in that case convalescence would be considerably prolonged. If, on the other hand, the infected uterus is left at rest, the virulence of the bacteria usually decreases;[15] and the fever, as a rule, disappears spontaneously, at times even quite rapidly. Involvement of the pelvic structures seems to be less frequent under this régime.

At any rate, it must be admitted that watchful waiting can do no harm. A death which occurs under conservative management, can probably not be prevented by active intervention. The latter carries with it also the danger of perforation with curette, dilators, placental or dressing forceps, and even the finger. The bleeding which to most physicians is an indication for immediate interference, is hardly ever copious enough to be alarming and can, moreover, be held in check by a skillful tamponade of the vagina which, in turn, encourages spontaneous expulsion of the infected tissues.

Which of these opposing plans of treatment are we going to teach our students, which shall we recommend to physicians? For, remember, this problem concerns the general practitioner quite as much as the obstetric specialist, because the great majority of septic abortions, in this country at least, is cared for outside of hospitals. One can readily imagine how confused a reader in search of information would be if he found in one textbook a definitely active therapy espoused and in another textbook an almost nihilistic conservatism advocated with equal positiveness. It seems to me that the American Gynecological Society because of its preeminence in the country, can render the medical profession a distinct service by endorsing a policy which would serve specialist and practitioner alike.

In proposing such a course of action, it might be well to bear in mind that every septic abortion is almost certainly a criminal abortion, that we are taking charge of a case without knowing the kind of infection and extent of traumatism inflicted, and that, if death ensues, we are likely to be blamed for the sins of the abortionist. This consideration should teach us caution and warn us against an overactive management. A wholly conservative attitude, on the other hand, is apt to meet with practical obstacles and opposition on the part of the patient.

The best mode of precedure is probably a compromise between the two extremes on principles of unification of treatment which may be

acceptable to everyone. With this end in view, I venture to submit the following theses to your discussion:

1. Every febrile abortion is potentially a serious condition which should be treated in a hospital.

At the present stage of our knowledge we are unable to foretell the virulence of the infection. Laboratory findings are only too often misleading. On the other hand, even a slight and apparently innocent elevation of temperature may be the forerunner of a grave sepsis; this was well illustrated in a case mentioned by Baer and Reis.[13]

2. Energetic systemic treatment is instituted at once. This consists of rest in bed, fresh air, forced feeding, alcohol, protein therapy (milk injections, blood transfusions), hypodermoclysis, etc.

3. The initial examination is made cautiously.

a. If there are definite complications outside of the uterus and even if there is only tenderness on palpation, strict conservatism must be observed. We then treat no longer the abortion, but its complications, and at most we may resort to quinine and pituitrin.

b. If ovular remnants protrude from the dilated cervix, they are pulled out with the placental forceps.

4. If a severe hemorrhage occurs at any time during the first two days, the vagina is gently packed with iodoform gauze, the end of the strip extending into the cervical canal.

5. If reexamination on the third day reveals no complication or tenderness outside of the uterus, curettage is performed irrespective of fever.

Proper operative technic is of decisive importance. The cervix is gently dilated in general anesthesia. The dilatation should be made with Hegar dilators, not with instruments of the Goodell type because with the latter, tears of the cervix are not always avoidable. The uterus is curetted quite lightly with a very large, sharp loop curette. The size of the instrument avoids the danger of perforation, particularly if, prior to the dilatation, 1 c.c. of pituitrin has been injected intramuscularly. The sharp curette, used in this manner, is far less violent than the blunt curette which requires much more force in dislodging placental remnants from the uterine wall.[16] The same objection applies to finger curettage, as it entails too much dilatation and a great deal of kneading and massaging of the uterus.

6. After evacuation, the uterus is kept contracted with ergot, and milk injections are continued until the fever has permanently disappeared.

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METROPOLITAN BLDG.

TUBERCULOUS SALPINGITIS

By CHARLES C. NORRIS, M.D., F.A.C.S., PHILADELPHIA, PA.

FIVE to ten per cent of all cases of salpingitis are of tuberculous origin. In the laboratory of Obstetrics and Gynecology at the University of Pennsylvania tuberculosis has been demonstrated in 7.7 per cent of all cases. In cases of tuberculosis of the female genital tract the tubes are affected in 90 per cent, the corporeal endometrium in 50 per cent, the ovary 40 per cent (oöphoritis 5 per cent, perioöphoritis 35 per cent), cervix 2 per cent, vagina 2 per cent, external genitals 1 to 2 per cent.

All cases should be viewed as secondary, although there are a few probably authentic primary cases recorded in the literature. Primary genital tuberculosis is so rare that many authorities deny its existence. Experimentation has shown that large numbers of virulent tubercle bacilli may be deposited in the vagina without the animal developing tuberculosis. When tuberculosis does develop, it is usually distant from the site of inoculation. The route of infection in these cases is generally through the pelvic lymphatics. The proportion of "takes" may be increased by a preliminary excoriation of the lining membrane of the vagina or by the production of a preliminary chemical or bacteriologic vaginitis. Even if this is done, the genital tract is relatively infrequently attacked although distal lesions may result. The wives of men suffering from tuberculous epididymitis rarely develop genital lesions despite the fact that virulent tubercle bacilli must frequently be deposited in the vagina with the seminal discharges. The fact that a few ascending infections do apparently occur as a result of laboratory experimentation and that a few rare instances of ascending genital tuberculosis have been observed in women should lead to precautionary measures being adopted by men known to be suffering from genital lesions. The fact of the matter is that even in these later cases other routes of infection are more likely than is the ascending one.

The tubes are generally the primary genital foci and the ampullas of the tubes the first portion attacked. The corporeal endometrium

is invaded in about half the cases and is probably often the result of extension from the tubes. Tuberculous endometritis is often somewhat irregular in its distribution, especially in the early cases, and the area surrounding the internal ostia is most frequently attacked. In some cases the endometrium is probably invaded at the same time as the tubes and in these is the result of a blood-borne infection. From the tubes the infection may spread to the peritoneum and result in a general peritonitis or less frequently the reverse may be the case. The well-established fact that the tubes are usually the primary intraperitoneal foci is of importance when considering the treatment of salpingitis. Preexisting inflammation is probably a predisposing factor to the development of tuberculous salpingitis.

Many cases of tuberculous salpingitis are of the unsuspected variety, Williams found 75 per cent were of this type. A study of our cases at the University of Pennsylvania showed that it was possible to make the diagnosis from the macroscopic appearance of the specimen or preoperatively in 25 per cent of cases, 50 per cent were suspected, and 25 per cent were entirely unsuspected prior to the histologic examination. In tuberculous infections of the tube the external abdominal ostia exhibit a tendency to remain open longer than in any other form of infection. This is especially the case when ascites is present. Tubercles may be visible upon the peritoneal coat of the tube and are practically always so when the condition is secondary to a general peritonitis. Cheesy or caseous material is present in the lumen of the tubes in advance cases and particles of this material may sometimes be attached to the fimbria. Tuberculosis sometimes results in the formation of nodular or small tumor-like enlargements, especially in the isthmus of the tube, the so-called salpingitis ischmica nodosa, although similar lesions may be observed in nontuberculous conditions. Histologically tuberculosis sometimes produces a picture which is superficially suggestive of carcinoma. The epithelium may be reduplicated, the cells irregular in size and staining properties and a false appearance of new gland formation may be present. The presence of tubercles is characteristic and the differentiation from carcinoma is easily made by an experienced pathologist.

A family history of tuberculosis may be present and a history suggestive of tuberculosis elsewhere in the body is generally obtainable. The lungs are the primary site in the majority of cases. A history of frequent "colds," chronic coughs, and pleurisy or of bone or joint lesions may be present. A period during which there has been a slight but unaccounted for evening rise in temperature is suggestive. In a certain proportion of cases there have been a previous general peritonitis usually of the ascitic variety. In some individuals the general health has been poor and they have been underweight for years. Careful questioning will often elicit the fact that there has been a

mild exacerbation of the primary lesion a few weeks or months prior to the development of the pelvic symptoms. Despite the fact that nearly all cases are secondary, occasionally no definite history suggestive of the primary lesions is obtainable. The onset is often insidious, and the course marked by moderate exacerbations and remissions. The resistance of tuberculous salpingitis to the ordinary expectant treatment usually employed for pelvic inflammatory disease is marked and may be the first point to suggest the etiology of the condition. Tuberculous salpingitis is nearly always bilateral, hence pain is present in both ovarian regions. Nausea, vomiting, tympanites, constipation, anemia, moderate leucocytosis and a shortened sedimentation time and the usual symptoms of a pelvic inflammatory disease are present in varying degrees. Irregular fever varying from 99° to 103° F. with its accompanying phenomena is the rule. All the symptoms are variable. In some cases the symptoms produced by the primary lesion overshadow those of the salpingitis. Amenorrhea or scanty, irregular or painful menstruation frequently precedes the onset of the pelvic symptoms. Persistent diarrhea is suggestive of an intestinal involvement.

Apart from the previous history of the case and the tendency of the disease to run a more or less chronic course despite treatment, tuberculous salpingitis should be suspected when there is an absence of the symptoms of gonorrhea or a previous pregnancy or when the lower genital tract is normal and presents no signs of an ascending infection. Salpingitis in the virgin is nearly always of tuberculous origin. Its bilateral character, tendency to resist the ordinary expectant treatment, poor general condition of the patient out of proportion to what would be expected from the pelvic lesion are all points suggestive of this variety of infection. The development of a subacute or chronic general peritonitis usually of the ascitic variety and evidence of a primary lesion elsewhere in the body are all more or less characteristic of tuberculosis. A small amount of free fluid is often demonstrable in the culdesac even in the early stages of the disease. In the gonococcal type of pelvic inflammatory disease the endometritis and cervicitis precede the salpingitis, whereas with tuberculosis the reverse is often the case; hence, in the latter variety leucorrhea may be absent or develop subsequently to the onset of the tubal lesions.

Treatment.—The primary focus must be accorded due consideration and even in those cases where no primary focus can be demonstrated due precautions should be instituted and the case treated as if a small quiescent lesion were known to exist. In this connection, it should be remembered that physical signs of a pulmonary lesion generally underestimate the extent of the disease. Practically all these cases are secondary and the hazards of operation, therefore,

greater than in the nontuberculous individual. As a result, indications for operation should be more pronounced than in the commoner varieties of salpingitis. Fortunately, in the group in which the tuberculous character of the infection is not suspected the primary focus is generally small and quiescent and these patients usually bear even ether anesthesia well. As the primary focus is usually in the lungs, anesthesia is an important factor. Here, if anywhere, spinal anesthesia possesses many advantages. Local anesthesia may be possible for some of the milder cases but the fact that many cases of tuberculous salpingitis present operative difficulties in the shape of dense adhesions and often massive adnexal lesions with matting together of the omentum and intestines make this form of anesthesia unsatisfactory for the average surgeon.

The tendency for the disease to resist all forms of expectant treatment, the frequency of the subsequent development of a general pritonitis and the fact that the tubes are usually the primary intraperitoneal focus call for their removal when this is not contraindicated by other existing conditions. When operation is necessary, conservative surgery should be performed. A panhysterectomy is rarely indicated. Bilateral salpingectomy should be the rule, and generally it is better to remove both tubes even if only one is macroscopically diseased. Sterilization of the patient is less disadvantageous in these than in other forms of salpingitis. The corporeal endometrium is attacked in about half the cases, hence a high supravaginal amputation with cauterization of the cervical canal from above is often necessary. Drainage adds to the likelihood of fistulas and should be avoided when possible. As in all forms of pelvic inflammatory disease operation is rarely indicated during the acute stage of the disease. A preliminary course of expectant treatment is nearly always advisable and in a proportion of cases is curative. In addition to the expectant treatment employed for the commoner varieties of pelvic inflammatory disease, certain special measures are advisable in those cases suspected of being of tuberculous origin. Rest, fresh air, sunshine, preferably at an altitude of from 3000 to 5000 feet, forced caloric diet, and whisky in the form of milk punches is indicated. Heliotherapy is especially valuable, but should not be pushed when acute pulmonary lesions are present. Dretzka[1] and Gauvain[2] emphasize the value of sunlight. Heliotherapy should be regarded as an adjunct but not as a specific treatment. There is no satisfactory substitute for sunlight but artificial light may be tried when heliotherapy is impossible. Carbon arc light is said to resemble sunlight most nearly and daily treatment with a diffuse carbon light may be given, beginning with half-hour exposures and gradually increasing the duration of the treatment. Some authorities follow with ultraviolet rays.

X-ray therapy has been employed for the treatment of pelvic and
peritoneal tuberculosis with good results. Siedamgrotzky[3] denies that
the x-ray possesses any bactericidal action upon the tubercle bacilli.
He attributes the beneficial effects obtained to the destruction of the
tubercles and tuberculous granulation tissue and its replacement by
a cicatrix. Martius[4] has reported the end-results secured in a series
of 28 cases. These he divided into two groups. Group I was com-
posed of 9 cases which were considered inoperable and were treated
by x-ray therapy. In Group II there were 19 cases, all of which were
submitted to operation. Of the inoperable cases 4 were cured, 4
improved and 1 died six months later of pulmonary tuberculosis.
Group II consisted of two classes, the first Group II-A consisted of
8 cases of which 6 were correctly diagnosed before operation and 2
in which the tuberculous character of the infection was suspected.
Of these 8 cases, 1 died shortly after operation, 3 succumbed sub-
sequently, 1 from pulmonary tuberculosis, 1 from general miliary tuber-
culosis and 1 from a tuberculous meningitis. Group II-B consisted
of cases in which the tuberculosis was unsuspected prior to opera-
tion. Of these, one died two years after operation from intestinal
tuberculosis; the remainder were either improved or cured. Cassidy[5]
reports 17 cases of pelvic or peritoneal tuberculosis treated with deep
x-ray, 10 were cured, 2 improved, in 3 there was no change and 2
died. Uter[6] has employed x-ray therapy and reports a series of 24
cases treated with satisfactory results.

Many cases are clearly inoperable and these should be treated by
hygiene, diet, fresh air, heliotherapy and x-ray as already indicated.
For the mild or suspected cases similar treatment is indicated, but
if improvement is not noted, removal of the intraperitoneal foci should
be performed without undue loss of time. All postoperative cases
should receive a routine course of hygiene, diet and heliotherapy.
X-ray therapy is worthy of a trial. The dosage of x-ray varies con-
siderably in different cases but is usually not sufficient to produce
amenorrhea, and a castration dose is not required.

RESULTS

Total number of cases followed for 2-19 years	40
Total number of cases treated by operation	33
Total number of cases of salpingitis alone	22
Total number of cases of salpingitis and general tuberculous peritonitis	11
Mortality, immediate and late, all cases	22 per cent
Mortality, expectant treatment alone, all cases	32 " "
Mortality, expectant treatment and operation	9 " "

Mortality Operative
Salpingitis .... 4 per cent
Salpingitis and general tuberculous peritonitis .... 18 " "

Mortality, Late, All Causes
Expectant treatment .... 18 per cent
Expectant treatment and operation .... 9 " "

Operative Morbidity
Average stay in hospital 26 days

Results as Regards Cures
Cured or improved, expectant treatment 50 per cent
Cured or improved, operative treatment 72 " "

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TWENTY-SECOND AND CHESTNUT STREETS.

FACTORS PREDISPOSING TO PYELITIS IN PREGNANCY

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THE effort placed before you in this paper is a preliminary report of a survey of the healthy pregnant and puerperal woman, in so far as the protective mechanism of her urinary tract is concerned.

We would emphasize the fact that, in this endeavor, we are in no way dealing with the active infection, "pyelitis."

In this study, covering a period of two years, we have attempted to carry our investigation through four main avenues:

1. Is there an interference with the proper ureteral and renal drainage?

2. Is there a constant ureteral and renal dilatation? If so, at what term does this begin; when does it reach the maximum; to what degree does this develop?

3. Is there definite stasis; at what term and in what degree does it occur?

4. What knowledge could be obtained of a potential infection?

The material used in this study consisted of seventy-eight women, forty-two in the antepartum and thirty-six in the puerperal state.

Of the antepartum subjects, fifteen were primiparae and twenty-seven multiparae. These patients were carefully chosen because the history, in each, was free of any evidence of renal infection.

The technic of the preparation of the patient was the same in all antepartum patients: Hospitalization for twenty-four hours previous

to examination, absolute rest in bed, forced water intake, the rectum emptied, vulva shaved, gynecologic scrub-up.

The investigation of the postpartum cases was necessarily delayed until such time as marked danger of infection to the genital tract had passed. Consequently our study in this series dates from the ninth to the twenty-fifth postpartum day.

The method of approach to our hypothetical questions was a detailed study from the urethral orifice to the pelvis of the kidney of each patient. The urethra was catheterized and a specimen of the bladder urine obtained for a complete analysis and cultural growth. The bladder was filled to capacity with a 6 per cent sodium iodide solution,

Fig. 1.—Cystogram in antepartum patient at seventh month. Shows a distortion of the bladder, characteristic of all antepartum women.

the patient placed in the exaggerated Trendelenberg position for ten minutes and a cystogram taken in this posture.

The Brown-Buerger cystoscope was introduced. The vesical neck, the ureteral orifices, and the bladder were closely studied for abnormalities. The ureters were then catheterized to the renal pelves with No. 5 French ureteral catheters. Specimens from the separate kidneys were taken for analyses and cultures. Following this, the renal pelves and ureters were filled with a 12 per cent sodium iodide solution and skiagraphed.

The iodide solution was injected slowly by syringe, both sides being filled simultaneously. No manometer was used. Great care was taken to inject slowly and to stop at the slightest evidence of pain. In this

way, we were able to obtain bilateral ureteropyelograms with but four instances of complaint upon the part of the patient.

The Urethra.—The urethra of the pregnant woman seemed to share with the rest of the pelvic organs in the marked general congestion. There existed a noticeable ease with which the cystoscope could be passed. In the postpartum woman the congestion had disappeared.

Bladder.—Other than the very pronounced changes occurring in the trigone, the bladder mucosa of the pregnant woman showed very few

Fig. 2.—Cystogram in postpartum case at eleventh day. In contradistinction to the antepartum bladder this picture shows a marked relaxation.

differences from that of her nonpregnant sister. The vessels were larger, fuller, and at times tortuous. Cystography revealed some very interesting and sometimes startling changes in the contour of the bladder (Fig. 1).

The postpartum bladder had already resumed the appearance of that of the nonpregnant woman as early as the ninth day. Cystography showed no distortion but considerable relaxation (Fig. 2).

Contrary to the findings of Gauss,[1] corroborated by Stoeckel,[2] Hofbauer,[3] and Luchs,[4] we were unable to demonstrate an insufficiency

of the ureterovesical valve at any stage of pregnancy or in any of the puerperal cases in our series.

Trigonum Vesicae.—This portion of the bladder in the pregnant woman presents a decided change from the normal. *Congestion* of the mucosa became apparent early—in multiparae at the eighth week, in primiparae the tenth week—as in all the pelvic organs it was progressive as pregnancy proceeded.

At about this same period of pregnancy a new feature began to make itself apparent. There was a lengthening of the vesical trigone from the urethrovesical orifice to the interureteric ridge and a broadening of the base at the triangle, so that in many cases the ureteral orifices were really further apart than in the bladder of the nonpregnant woman. The impression obtained at cystoscopy was that a crowding upward of the trigone occurred, giving less room than usual. This was so pronounced in a number of cases that the cystoscope passed through the urethra directly on to the trigone, so that the catheterization of the ureters had to be performed from a considerable distance.

The elevation of the trigone was most noticeable along the interureteric ridge, which stood out with unusual prominence. The floor of the bladder fell away from the ridge rapidly and acutely, so that it became a valley, or even a bas fond. Perhaps this fact is responsible for the statement of Curtis[5] that a residuum exists in the bladder of the pregnant woman. Although we encountered no such finding in our series, it is not difficult to understand that in a certain percentage of cases a residual urine may occur, especially in the last trimester of pregnancy when the congestion, elevation and elongation of the vesical trigone are most pronounced.

The Ureteral Orifices presented no change from the normal, except as noted above; they frequently were more widely separated than usual, due to the broadening of the trigone. Ureteral catheterization presented no difficulty whatever from the ureteral orifice to the renal pelvis.

While the hypertrophy and hyperplasia of the muscle fiber and fibrous connective tissue, as put forward by *Hofbauer* in his recent monograph, may or may not completely involute as early as the ninth postpartum day, cystoscopic visualization of the bladder and trigone, at this date, showed a complete disappearance of the congestion, elongation, and elevation noted in the antepartum cases.

Bladder Urine.—The catheterized bladder urine in both antepartum and postpartum series showed no gross abnormalities. In our complete investigation of seventy-eight cases, albumin was present in but four; casts were found in only two.

TABLE I. BLADDER URINE

MICROSCOPIC AND CULTURAL GROWTH	ANTEPARTUM (PER CENT)	POSTPARTUM (PER CENT)
White blood cells	40.0	61.0
Frank pus	2.4	19.0
Coliform organisms	12.0	13.0
Coccal organisms	45.0	66.0
No growth	20.0	19.0

Microscopic examination and cultural growth of the catheterized bladder urine of pregnant and puerperal women presented, to our minds, definite findings, which were entitled to thorough study.

We were impressed with the large percentage of the occurrence of white blood cells. In our series we will consider the presence of white blood cells in the urine, when not due to blood, as clinical evidence suggestive of infection. Table I demonstrates a 42 per cent incidence of infections in the antepartum cases, which rose in the postpartum ones to 80 per cent.

The most surprising finding in the cultural growths was the evidence of some variety of the coliform bacillus in these apparently healthy pregnant and puerperal women. The presence of these bacilli must be taken seriously. The very fact that they were found indicates that they are making their way into the bladder from some source.

Regarding the coccal infections, which are usually considered as contaminations of technic, their high incidence in our series makes us regard them with suspicion and worthy of more extended investigation.

TABLE II. URETERAL URINES

	ANTEPARTUM		POSTPARTUM	
	RIGHT URETER (PER CENT)	LEFT URETER (PER CENT)	RIGHT URETER (PER CENT)	LEFT URETER (PER CENT)
White blood cells	23.8	9.0	8.0	11.0
Frank pus	0.0	2.4	2.7	2.7
Coliform organisms	9.0	9.0	2.7	11.0
Coccal organisms	50.0	35.0	61.0	29.7
No growth	56.0	47.0	36.0	63.0

Microscopic examination of the urines from both kidneys shows in the presence of white blood cells and frank pus, a marked decrease when compared with the same picture of the bladder urine.

Whereas a study of the coliform organisms demonstrated the persistence of these bacteria in the kidney urine in but a slightly lowered percentage. This would lead us to infer that a combined cultural study of the bladder and ureteral urines indicates a potential renal complication.

Of interest in this series was the occurrence of pyelitis in four cases, making its appearance in the earliest case three weeks after cystos-

copy. Three cases developed prenatally, one in a primigravida, two in the multigravidae. One demonstrating the attack, on the tenth postpartum day, was in a multipara. Everyone of these cases gave a positive coliform growth in the ureteral and bladder urines at the time of cystoscopy.
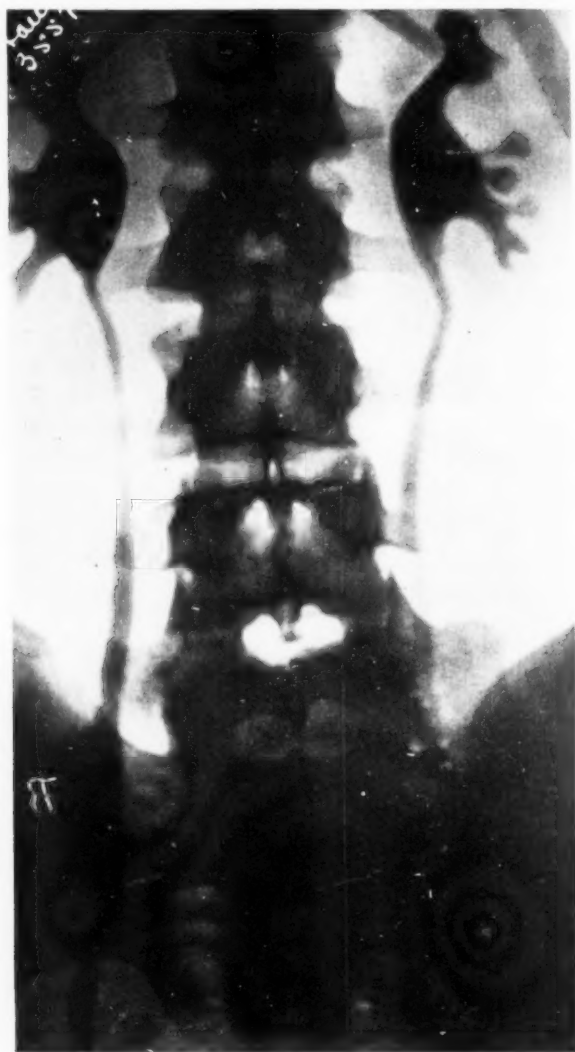
Fig. 3.—Ureteropyelogram, bilateral, in antepartum multipara at the sixth week. This shows early beginning dilatation of the ureters and renal pelvis. Note the absence of abbreviation in the lower ureters.

URETERAL DILATATIONS

Ureteral dilatations occurring during pregnancy have been fully recognized and freely discussed in the literature. Cruveilhier[6] was the first to observe ureteral dilatation in women dying during the

latter months of pregnancy and in the puerperium. Olshausen,[7] Prutz,[8] Lohlein,[9] Carson,[10] and others have made similar contributions to the literature. All these workers studied the autopsied woman. Kretschmer and Heaney,[11] Crabtree,[12] Pugh,[13] Corbus and Danforth,[14] and Hunner[15] are among those who have used the living subject for their observations.
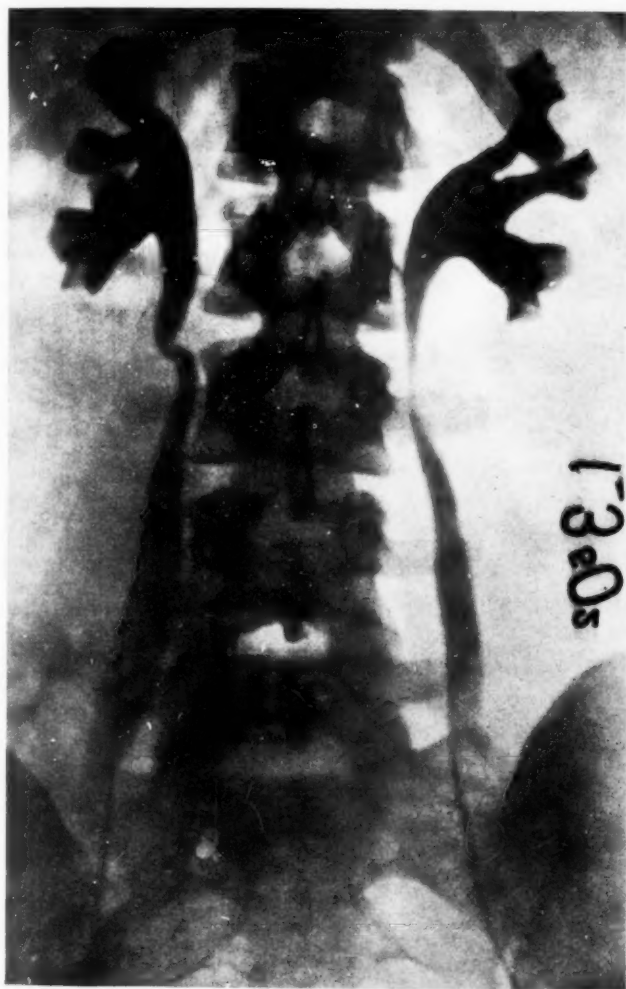
Fig. 4.—Ureteropyelogram, bilateral, in antepartum primipara at the tenth week. This shows a well-defined dilatation in both ureters with beginning hydronephrosis. Note the distinct abbreviation in the lower ureterograms.

Our effort will be to determine the earliest moment of onset in the primipara and multipara, with a comparison between the two. Secondly, to estimate the character of its progress with regard to the period of pregnancy. Finally, to determine whether or not this condition is persistent in the postpartum period.

TABLE III.   URETERAL DILATATION

| | ANTEPARTUM | | POSTPARTUM |
	PRIMIPARA (PER CENT)	MULTIPARA (PER CENT)	(PER CENT)
Right	100.0	100.0	86.0
Left	66.6	77.0	63.8
Bilateral	66.6	77.0	66.6
No dilatation right			13.8
No dilatation left	33.3	23.0	36.1

Dilatation of the ureter was noted by us as early as the sixth week in multiparae and at the tenth week in primiparae.

With regard to the character and progress of the dilatation, and considered at the different periods of pregnancy, our experience seems to show that dilatation, while appearing very early in both primiparae and multiparae, does reach its maximum shortly; at the twenty-fourth week in primiparae and the twenty-second week in multiparae. The amount of sodium iodide solution which could be injected into the ureter without pain did not vary to any extent, whether in early or late pregnancy. It may be stated that upon no occasion was an effort made to instill more than thirty cubic centimeters of the iodide solution. The average amount used by us in our experiments was fifteen cubic centimeters. Ureterograms made with thirty cubic centimeters in no way showed a greater degree of dilatation or a better definition. Our studies have impressed us more with the "tissue factor" of each individual woman.

Further, the multiparous woman demonstrated dilatation earlier in pregnancy than the primipara. In both parities the right ureter exhibited some degree of hydroureter in every instance. In left-sided and bilateral hydroureter the multiparae showed a greater frequency of dilatation than the primiparae. The more pronounced types of hydroureter were found in the multiparae. We have been impressed with the possible fact that the ureter, like the perineum, having once been dilated, particularly as in .pregnancy over a period of many weeks, involutes apparently to normal but in a relaxed state.

The study of the ureter in thirty-six cases, from the ninth to the twenty-fifth postpartum day, reveals the fact that while involution has taken place rapidly in a minority of these cases within these time limits, there still remains a great majority showing right, left, and bilateral dilatation. In fact we have ureterograms of two cases which demonstrate this persistence, in the absence of disease, over periods of twenty-one months and nine years.

URETERAL DISTORTIONS

Beginning at the sixteenth week the antepartum differed from the postpartum ureter in the abrupt termination of the ureterogram at the level of its entry into the parametrium. On the other hand the

Fig. 5.—Ureteropyelogram, bilateral, in antepartum multipara at the sixteenth week. This shows a marked dilatation and redundancy of the right ureter with a moderate hydronephrosis. Left ureter not dilated. Abbreviation of right ureter again noted.

postpartum ureter could easily be traced to the bladder; in fact, a dilatation of this lower third was in certain instances demonstrated.

Redundancy and kinking of the ureter, while a very definite finding in both antepartum and postpartum cases, was met much more frequently and in greater degrees in the prenatal skiagraphs.

An appreciable stricture revealed itself but once in this whole series of one hundred and fifty-six ureters. This one case was found in the left ureter of a postpartum woman.

The same observation made concerning hydroureter may be largely

Fig. 6.—Ureteropyelogram, bilateral, in antepartum primipara at the twenty-eighth week, showing a dilated right ureter and hydronephrosis. Note the ureteropelvic kink. Note bilateral abbreviation.

applied to hydronephrosis. It begins as early as the sixth week in multiparae and the tenth in primiparae and reaches its maximum at the twenty-fourth week in primiparae and at the twenty-second week in multiparae.

TABLE IV. HYDRONEPHROSIS

| | ANTEPARTUM | | POSTPARTUM |
	PRIMIPARA (PER CENT)	MULTIPARA (PER CENT)	(PER CENT)
Right	93.0	96	72.2
Left	46.2	66	52.7
Bilateral	46.5	62	44.4
No dilatation right	6.6	3	27.7
No dilatation left	53.8	33	47.2

Referring to Table IV, the frequent incidence of hydronephrosis in primigravidae and multigravidae and the postpartum patient is emphasized. The continued predominance of right-sided dilatation is very evident. Left pelvic dilatation, while not quite so frequent in occurrence as left hydroureter, developed in a large proportion of the three groups. The same remarks may be made of the ratio of bilateral dilatation. The escape of the left renal pelvis, to an even greater degree than the left ureter, must be remarked because of the recognized frequency of right-sided pyelitis.

A marked pelvic dilatation on the right side in primiparae was found in 73.2 per cent, in multiparae in 81 per cent, in the postpartum in 55.5 per cent. The same degree of dilatation on the left in primigravidae in 33 per cent, in multigravidae in 40 per cent, in the postpartum in 27 per cent.

Marked hydronephrosis was found much more frequently in the multiparous woman.

While the hydronephroses in our series of antepartum and postpartum women have been well defined and even marked dilatations, in no case have we noted the extreme pelvic distension mentioned by other authors. The largest amount of urine recovered in our series was sixty-seven cubic centimeters, the average being five. Possibly these very much over-dilated renal pelves reported by others were associated with some degree of infection. Dilatation to the extent of thirty to four hundred and eighty cubic centimeters of urine recovered has been reported by Crabtree. There is a very evident recovery of the pelvic tone early in the period of general postpartum involution. In this survey of the postpartum patient, which extended up to the twenty-fifth day, there is a persistence on the right side of pelvic dilatation in 72.2 per cent and on the left of 52.7 per cent of our cases. An impression derived from this fact, emphasized by Helmholtz,[16] leads us to believe that the dilatation produced in a first pregnancy must have an influence in the production of the greater frequency and the more marked degree of dilatation found in multiparae.

STASIS

In our investigation of this very important factor in the development of pyelitis, we have a series of twenty antepartum and twenty-six postpartum cases.

Our technic has been that developed by Goldstein.[17]   Skiagraphs were taken immediately, and at seven, ten, fifteen, twenty, thirty,

Fig. 7.—Ureteropyelogram, bilateral, in antepartum multipara at the twentieth week, showing very distinctly, bilateral ureteral dilatation with right hydronephrosis.   It illustrates the abbreviation at the pelvic brim and also the separation of the ureters.

forty-five and sixty minutes after the instillation of sodium iodide solution into the ureters and renal pelves.   In antepartum cases our observations revealed that the left ureter and renal pelvis emptied themselves within the normal limits of seven minutes with double the frequency of the right.

Conversely, it was discovered that, in the actual stasis from the mild degree of fifteen minutes, through the moderate type of thirty min-

utes to the marked group of sixty minutes delay, the right side out-numbered the left in the proportion of four to three.

We would emphasize the fact that, in the class of one hour's stasis, the right side outnumbered the left in the proportion of two to one.

In averaging the time occupied by the two sides in their efforts to empty themselves, we have found that the right side required thirty-seven minutes, the left twenty-nine.

Fig. 8.—Ureteropyelogram, bilateral, of the same patient as shown in Fig. 7. This was taken twenty minutes after the injection of the iodide solution. It shows some emptying.

While ureteral dilatation and hydronephrosis usually appear and reach their maximum relatively early in pregnancy, stasis, however, does not make its appearance until the twentieth week. Whether it is acute or gradual from the onset to the development of an hour's

retention, we are unable to state, not having had the privilege of following a single case from its inception to the termination of gestation. We may state that several of our cases from the twentieth to the twenty-sixth week of pregnancy have shown a delay of one hour; conversely, we have had several instances in women at full term completely emptying the ureters and pelves in less than thirty minutes.

Fig. 9.—This photograph is of the same patient as shown in Figs. 7 and 8. It will be seen that after sixty minutes there is a trace of the iodide solution in the pelves and ureters.

It has been our experience that the multiparous woman presents more frequent, earlier, and greater degrees of stasis than the primiparous patient.

A comparison of stasis between the antepartum and postpartum series presents striking and interesting differences. The postpartum

patient requires but one-half the average time to empty the renal
pelves and ureters completely.   There was no appreciable difference in
the time demanded by either side.   There was no retention beyond forty-
five minutes.   In fact the majority were completely empty within fif-
teen minutes.   In the antepartum series we found that 30 per cent of
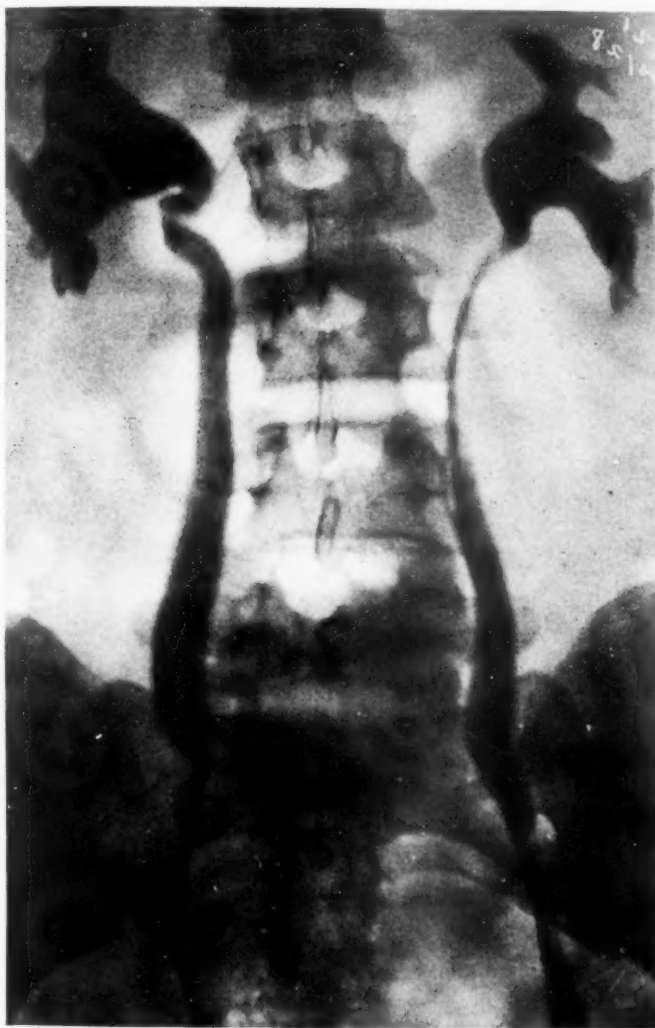
Fig. 10.—Ureteropyelogram, bilateral, in postpartum primipara at the twelfth day.
This shows a marked dilatation of the right ureter with redundancy and hydronephro-
sis.   The left ureter is also dilated.   Note some degree of dilatation in both lower
ureters.

the ureters and pelves emptied themselves within the normal limit of
seven minutes, whereas in the postpartum 38 per cent were empty in
the same period of time.   In the former group but 10 per cent were
empty in from seven to twenty minutes whereas in the latter group 42

per cent were evacuated within the same time limit. In the more marked type of stasis from thirty to sixty minutes we have in the prenatal class 60 per cent which showed this great delay. Opposed to this latter figure we have in the postpartum series in the same group but 9 per cent which demonstrated a delay up to and including forty-five minutes.

Fig. 11.—Same patient as shown in Fig. 10. Taken seven minutes later. Shows retention in right ureter, left empty.

There were no postpartum cases showing stasis up to sixty minutes.

The inference to be drawn, we think, from this exhibit is that the uterus and its contents, in spite of DeLee's statement, must play some part in maintaining stasis. All these postpartum skiagraphs were taken at or before the twelfth postpartum day.

One can hardly conceive that the involution of the ureter and its return to the normal tone, peristalsis and drainage within these time

limits could be accomplished so rapidly. In fact unless the trauma of labor produced an edema in the ureter itself, stasis seemed to be relieved greatly following the birth of the child.

An interesting point exhibited by our examination was the apparent complete disappearance of the emphasized abbreviation of the dilated ureter at or near the pelvic brim, noted in the antepartum cases.

The ureter of the postpartum woman, in contradistinction to the
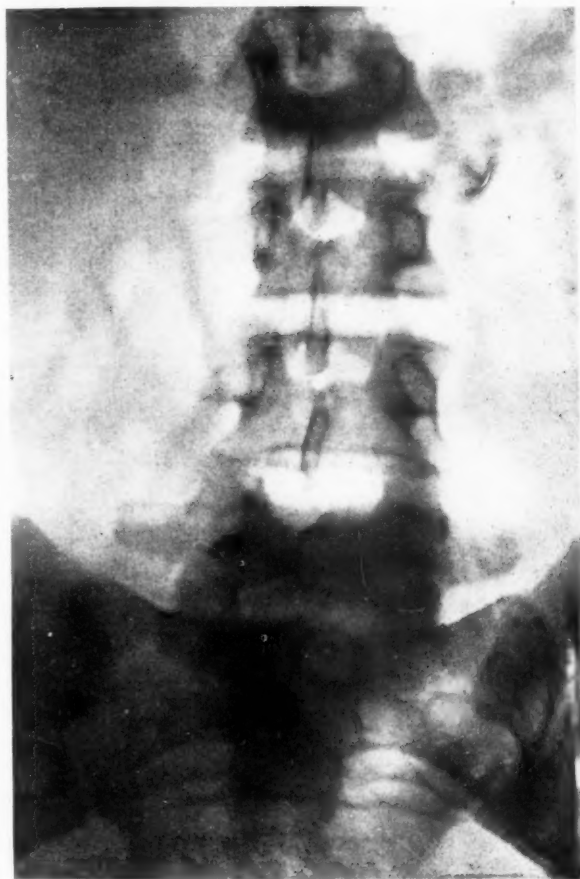
Fig. 12.—Same patient as shown in Fig. 10. Taken fifteen minutes after injection of iodide solution. Both ureters and pelves empty.

antepartum, shows varying degrees of dilatation of its juxtovesical portion. These findings, we think, confirm in the living subject Carson's conclusions on pressure at the pelvic brim demonstrated on the cadaver.

DISCUSSION

Is there an interference with the proper renal and ureteral drainage? We believe that there is. Beginning in the fetus of six months and

in the full-term newborn child, we have found consistently by a histologic study that the ureteropelvic portion of the ureter shows a moderate amount of muscle and fibrous connective tissue, the middle third a less amount, whereas the pelvic and intravesical portions present a more marked degree of the same.

We believe that this reinforcement of the upper third of the ureter is primarily to produce peristalsis but at the same time, perhaps, also to protect the renal pelvis to some degree from regurgitation; the same contention may be applied to the similar occurrence in the lower third, only in a more pronounced manner.

The dilatability of the middle third of the ureter is, up to certain limits, physiologic and only tends to become pathologic, in our opinion, when the musculature of the ureter as a whole becomes atonic.
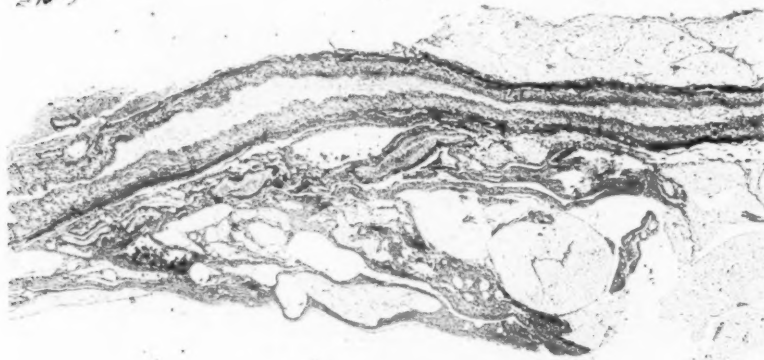
Fig. 13.—The muscle and fibrous connective tissue reinforcement of the juxtovesical portion of the ureter of a fetus of six months' pregnancy is demonstrated. The physiologic dilatation of the middle third is also shown.

Many authors have described the lower third of the ureter in detail; the established fact of the presence of a much greater amount of muscle and fibrous connective tissue in this part of the organ is accepted by all. In his recent and most interesting monograph, Hofbauer has demonstrated in pregnant women an increase in the muscle and fibrous tissue of the whole ureter, but more particularly in the juxtovesical and intravesical portions. While one is prepared to accede some responsibility for the actual development of hydroureter and hydronephrosis in pregnancy to this hyperplasia and hypertrophy, it would seem impossible to concede to it, according to Hofbauer's interpretation, the position of the greatest factor in the development of these conditions.

We prefer to interpret this hypertrophy and hyperplasia as one of physiologic development, for the purpose of protection and of adding to the ureter a greater power to accomplish successfully a larger amount of work.

Graves and Davidoff[18] by their experiments upon the peristaltic action of the ureter have exhibited the fact that the pacemaker for peristalsis in the ureter really lies in the pelvis of the kidney, where a definite head of pressure is maintained. In so far as the upper third of the ureter maintains the same rate and strength in the peristaltic wave and the lower third harmonizes by forcing the urine into the bladder, this head of pressure is maintained at an even level.

Fig. 14.—This shows the blood supply of the nonpregnant uterus.

At the instant of obstruction in the ureter this even mechanism is disrupted and there is immediately produced an elevation in the renal head of pressure, with a consequent increased amount of tension in the walls of the renal pelvis and the ureter itself. Crabtree reports a rise of from five to seventy-five millimeters of mercury in the renal pelvis in one hour in complete obstruction.

The primary result of beginning obstruction in the ureter is a physiologic dilatation. Depending upon the character of the muscle and fibrous connective tissue, which develop an immediate hypertrophy to meet this new demand, the obstruction will be overcome and the physiologic drainage will continue, or continued overdistension will result. This, to our minds, will bring about a definite loss of tone in the ureter, which will be reflected upon the renal pelvis. Stasis, such as we have shown, will be the inevitable result. We prefer to consider

the hypertrophy and hyperplasia as described by Hofbauer as a result of primary physiologic overdistension rather than the cause of obstruction.

What, then, may be the factors in pregnancy which are likely to produce some obstruction in the ureters giving rise to a hyperplasia and hypertrophy in these structures.

The first probable factor is an increased vascularity in the cervix and parametrium with its pressure capacity and consequent production of congestion.

Secondly, comes the pressure from the general pelvic overcrowding of the growing uterus, which develops equally and in all dimensions,

Fig. 15.—This shows the enormous increase in the vascularity of the uterus at eight weeks of pregnancy.

as exhibited upon the bowel, the bladder, and consequently must produce an effect upon the ureters themselves.

Thirdly, a marked congestion and distortion of the vesical trigone.

Finally, the well-recognized dextrorotation of the uterus.

To these combined physiologic forces we believe is due the physiologic hyperplasia and hypertrophy found in the ureter in pregnancy.

In our study, one of the outstanding impressions has been what we have chosen to call "the tissue factor." The variations in ureteral and renal dilatations have not been impressively synchronous with the period of gestation. We have noted as many marked dilatations in the early weeks of pregnancy as in the later months. From this we

conclude that our different cases have developed this peristaltic power of the ureters in varying grades, and consequently demonstrate hydroureter and hydronephrosis in different degrees, according to their tissue factors.

CONCLUSIONS

Physiologic forces external to the ureter cause obstruction to ureteral and renal drainage in pregnancy, which is relieved almost immediately upon the termination of gestation.

2. In pregnancy, there is a constant right-sided ureteral dilatation; while right hydronephrosis is only slightly less frequent.

3. In pregnancy, the left ureter and renal pelvis escape this dilatation in a markedly higher percentage of cases.

4. Bilateral hydroureter and hydronephrosis were of very frequent occurrence.

5. The multiparous woman showed these conditions earlier, more frequently, and in much more marked degree than the primipara.

6. Stasis, as measured by inability of the renal pelvis and ureter to empty themselves within the normal time limits, is a definite and almost universal finding in the antepartum woman. In the postpartum woman it is still persistent, in a lesser degree, over a prolonged period of time.

7. By the demonstration of an unexpected amount of pus and coliform organisms in the bladder and kidney urines of these supposedly healthy pregnant and postpartum women, we believe there is some justification for the use of the term, "a hidden infection."

8. Every pregnant woman has obstruction of some degree, a definite dilatation of the ureters and renal pelves, with a well-defined stasis. This continues over a long period of time. We have demonstrated in the apparently healthy pregnant and puerperal patient a probable renal complication, the presence of pus and coliform organisms. The line of demarcation between the physiologic and the pathologic in these cases is a very fine one. Trauma and a lowered immunity or resistance are the remaining factors needed.

These women, in our opinion, are all subjects for a possible pyelitis.

We would like in conclusion to express our deep debt of gratitude to Dr. P. J. Kearns of the Pathologic Department and to Dr. W. W. Beattie of the Bacteriologic Department of the Royal Victoria Hospital, Montreal.

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MEDICAL ARTS BUILDING.

EPIDERMOID CARCINOMA OF THE CERVIX UTERI

A HISTOLOGIC STUDY TO DETERMINE THE RESEMBLANCE BETWEEN BIOPSY SPECIMENS AND THE PARENT TUMOR OBTAINED BY RADICAL PANHYSTERECTOMY

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SINCE the publication of our observations[1,2] on the relative malignancy of cancer of the cervix uteri as indicated by the predominate type of cancer cell, efforts have been made by some radiologists particularly Schmitz,[3] Pomeroy and Strauss,[4] Böhm and Zweifel[5] and others to predict from the histologic appearance of biopsy material the predominant type of cancer cell, composing the entire tumor. On such a basis, due consideration being given to the clinical local extent of the disease, these radiologists have felt able to judge of the apparent malignancy of the uterine neoplasm and with a fair degree of accuracy to anticipate the outcome in patients treated by radium.

This study was therefore undertaken to ascertain the degree of resemblance between cancer cells observed in small pieces of tissue obtained for diagnostic purposes and the cancer cells observed in numerous microsections obtained from various portions of the parent tumor.

Such a determination would appear timely since in some clinics radium is being used to the exclusion of surgery for cancer of the cervix uteri. This means that the entire parent tumor no longer becomes available for study while histologic data are obtained from small biopsy specimens.

Also in cases where radium is used as a preoperative measure the appearance of cancer cells is sometimes so altered in the operatively removed uterus that it would appear useful here to know how valuable biopsy material is in reflecting the predominant type of cancer cell composing the parent tumor.

A brief recapitulation may not be amiss to summarize our published work previously referred to. This concerns itself with our demonstration that epidermoid cancers of the cervix uteri can generally be grouped according to the predominant type of cancer cell composing the tumor. We were able, in our previously reported studies, to recognize three fairly distinct cell types in our cancer material. These we designated as the *spinal*, *transitional*, and *spindle* types of cancer cell. As has been previously noted, all combinations of cell types occurred, but irrespective of the occurrence of other cell types we were able to show that the predominant type of cancer cell indicated with a fair degree of accuracy the relative malignancy of the tumor as determined by its invasiveness and its curability by operation. Our findings as compared with those of Broders are summarized in Table I.

TABLE I. PERCENTAGE INCIDENCES OF "FIVE-YEAR OPERATIVE CURES" FOR THE DIFFERENT TYPES OF EPIDERMOID CANCER OF THE CERVIX UTERI

	SPINAL-CELL CANCER (GRADE II OF BRODERS) PER CENT	TRANSITIONAL-CELL CANCER (GRADE III OF BRODERS) PER CENT	SPINDLE-CELL CANCER (GRADE IV OF BRODERS) PER CENT
The Johns Hopkins Hospital (Martzloff)*	47.00	24.2	9.5
The Mayo Clinic (Broders: Personal Communication)	53.33	21.5	9.52

*Martzloff: Johns Hopkins Hosp. Bull., March, 1927, xl, 161.

A brief description of the cancer cells described in our earlier study is as follows:

The *spinal type of cancer cell* resembles the cells seen in the superficial portion of the normal stratified cervical epithelium (Fig. 1, *a*), being polyhedral in shape, with a well-defined cell membrane and a fairly large nucleus. The nucleus assumes only a moderately intense hemotoxylin stain while the cytoplasm which is abundant takes a rather pale eosin coloration (Fig. 2).

The *transitional type of cancer cell* resembles somewhat a more deeply situated group of cells seen in normal cervical epithelium. (Fig. 1, *b*.) The cancer cells have a very faint or indefinite cell membrane while the cytoplasm is less abundant and more deeply staining than in the spinal type of cancer cell. The nuclei take a deep hemotoxylin stain and generally have nucleoli. (Fig. 3.)

The *spindle type of cancer cell* is, as its name implies, spindle-shaped. For the sake of brevity this description will suffice, for it serves to identify the cell type under consideration. (Fig. 4.)

In a more recent study[6, 7] we have shown the factors that apparently govern operability in the various cell types of cancer and have indicated the prognosis that may be anticipated in a group of operative cases from a consideration of the clinical aspects and an adequate study of the pathologic specimens. Table II briefly summarizes these deductions.

TABLE II. SHOWING THE PROGNOSIS THAT MAY BE PREDICTED IN PATIENTS SURVIVING OPERATION WHEN CONSIDERATION IS GIVEN THE FACTORS GOVERNING OPERABILITY AND THE PREDOMINANT TYPE OF CELL COMPOSING THE CANCER

TYPE OF CANCER	NUMBER OF CASES	NO. HISTOLOGICALLY BEYOND SCOPE OF PERMANENT CURE (INOPERABLE)	NUMBER OPERABLE	NUMBER CURED	PER CENT OF OPERABLE CASES CURED
Spinal-cell	30	8	22	14	63.6
Transitional-cell	90	44	46	18* (22)	39.1* (47.8)
Spindle-cell	17	10	7	1	14.0
Total for epidermoid cancers	137	62	75	33 (37)	44.0 (49.3)
Adenocarcinoma	9	5	4	3	75.0
Total	146	67	79	36 · (40)	45.5 (50.0)

*To this number might well be added four other patients who were operable and died or were lost 7, 8 and, in two instances, 10 years after operation without evidence of recurrence. This would then yield the results indicated by the figures in parentheses.
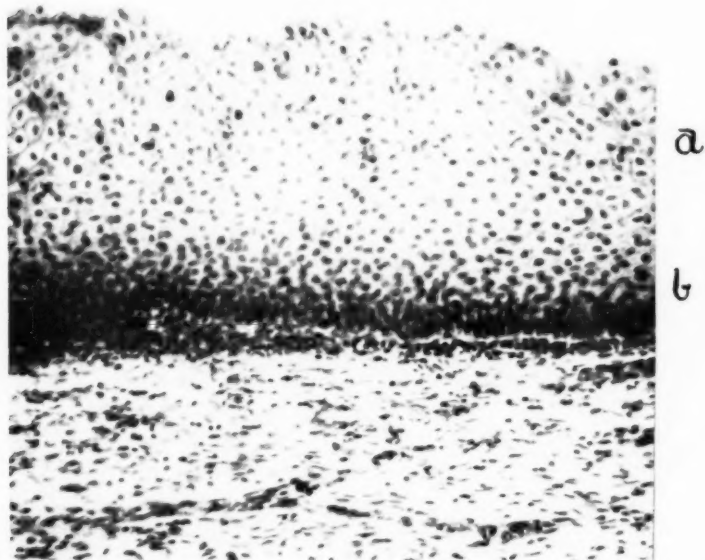
Fig. 1.—Normal cervical epithelium. At *a* are the so-called spinal cells with distinct cell membranes and abundant pale eosin staining cytoplasm. At *b* are the so-called transitional cells where no distinct cell membrane is seen, the cytoplasm is less abundant and all portions of the cell take a deeper stain.

If one wishes to apply the above data to the pathologic evidence obtained from biopsy material, it then appears essential to know as a minimal requirement how valuable biopsy material may be in its ability to reflect the cytomorphology of the parent tumor.

For the purpose of this study we have 70 specimens removed from patients who were on the gynecologic service of the Johns Hopkins Hospital. All of these patients had unmistakable cancer of the cervix

uteri. In each instance tissue was removed from the cervix either several days prior or immediately preceding the major operative procedure. The local removal of tissue was followed by immediate radical cauterization of the cervix in practically every patient.

Fig. 2.—Spinal-cell cancer.

Fig. 3.—Transitional-cell cancer.

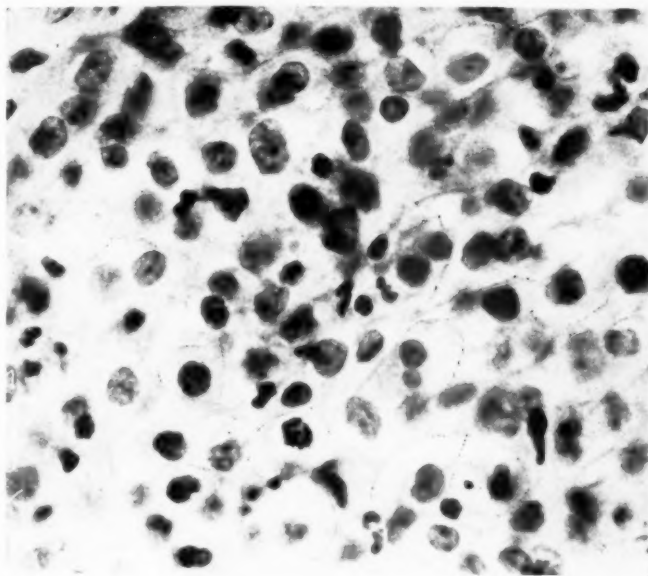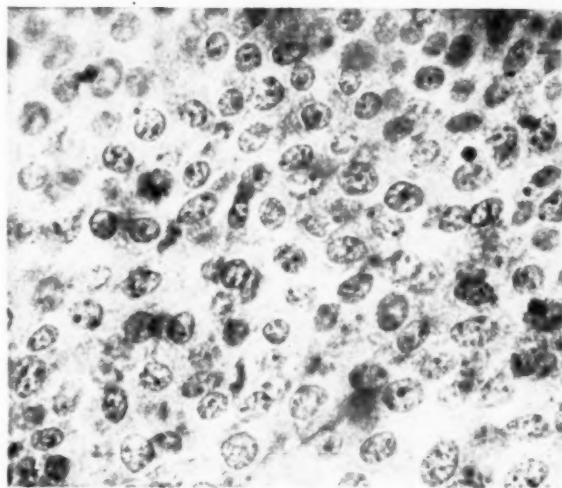As in our previous publications we are again designating these cancers by the predominating variety of cancer cell; viz., the transitional-cell, spinal-cell and spindle-cell groups. In addition, for this study, we have segregated a fourth group in which the spinal and

transitional cancer cells occur in about equal proportions. This latter group in previous reports has been incorporated with the transitional-cell group in order to simplify what might otherwise have become a cumbersome division of material and, I might add, has served to swell the number of cures in the transitional-cell type of cancer.

Under the four above-mentioned groups the biopsy material and the corresponding parent tumor have been compared as to their content of various cell types, the occurrence or absence of epithelial pearls,
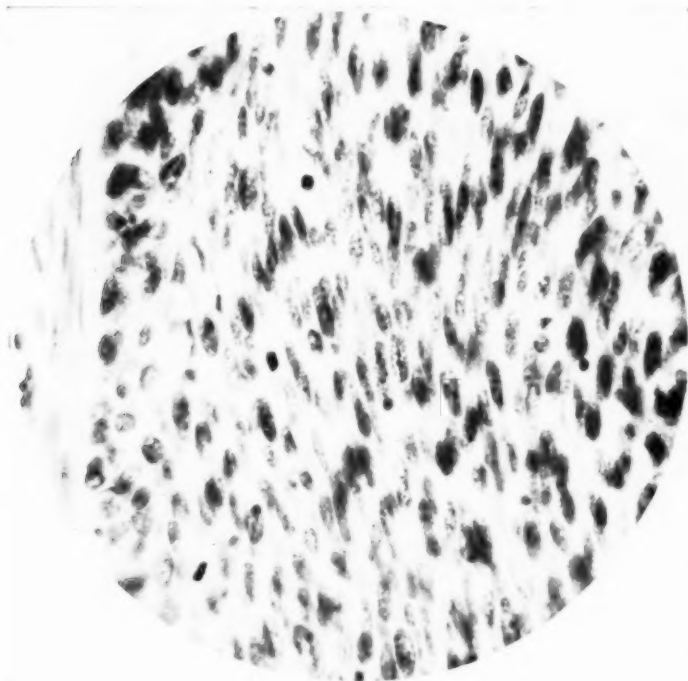
Fig. 4.—Spindle-cell cancer.

giant cells, nucleoli, and mitotic figures. Finally the general histologic pattern was compared where sufficient tissue was present in the biopsy material to warrant such a contrast.

TRANSITIONAL-CELL CANCER

For our present study 43 specimens of transitional-cell cancer were available. As we have previously reported, cancers in which this type of cancer cell is the predominating variety formed the great majority of malignant cervical neoplasms encountered.

It will become apparent in the analysis of this material that while the transitional cell is the predominant variety, both the spinal- and spindle-cell types of cancer cells commonly occur with varying frequency. It would lead too far afield and afford complex data of ques-

tionable value for this particular study to enumerate for these or the following groups of tumors the incidence with which other varieties of cells occur in noteworthy numbers. However, merely for illustration it can be said that of the 43 cases in this group 32 (74.8 per cent)
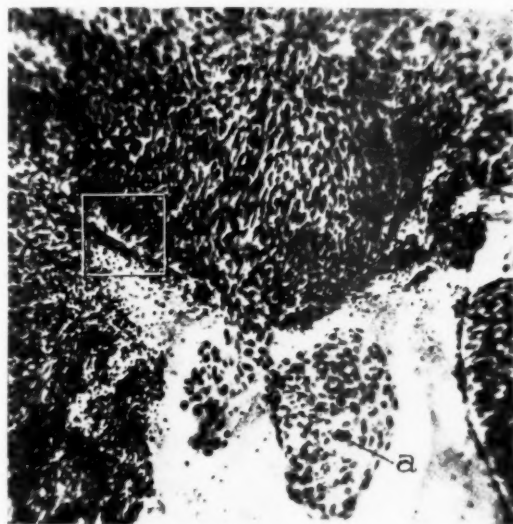
Fig. 5.—(Gyn. Path. No. 27069.) Biopsy showing predominance of spindle type of cancer cell. At *a* is a multinuclear giant cell.
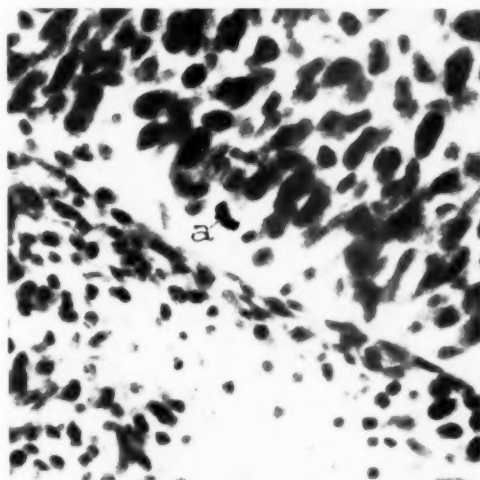
Fig. 6.—(Gyn. Path. No. 27069.) High power view of blocked area in Fig. 1. At *a* is a mitotic figure and elsewhere there are round and oval cells verging on spindle shape. From such an area no conclusion can be drawn as to the predominant type of cancer cell.

showed the spindle type of cancer cell in sufficient number to make it a factor in the histologic picture. In instances where cancer alveoli showed occasional peripherally situated spindle cells in numbers so

small as hardly to influence the histologic panorama, their occurrence
was not noted. Had notation been made of these then the above
incidence would be entirely too small. The same may be said for the
occurrence of spindle cells in association with spinal-cell cancer,
though here the generalization cannot be so sweeping. On the other
hand no such generalization can be made for the association of spinal
cells in tumors predominately of the transitional-cell type. Here we
found typical spinal cells in 17 instances (39.5 per cent) while in 7
more specimens cells occurred that could questionably be classified as
spinal cells. In the later specimens these cells had in many areas the
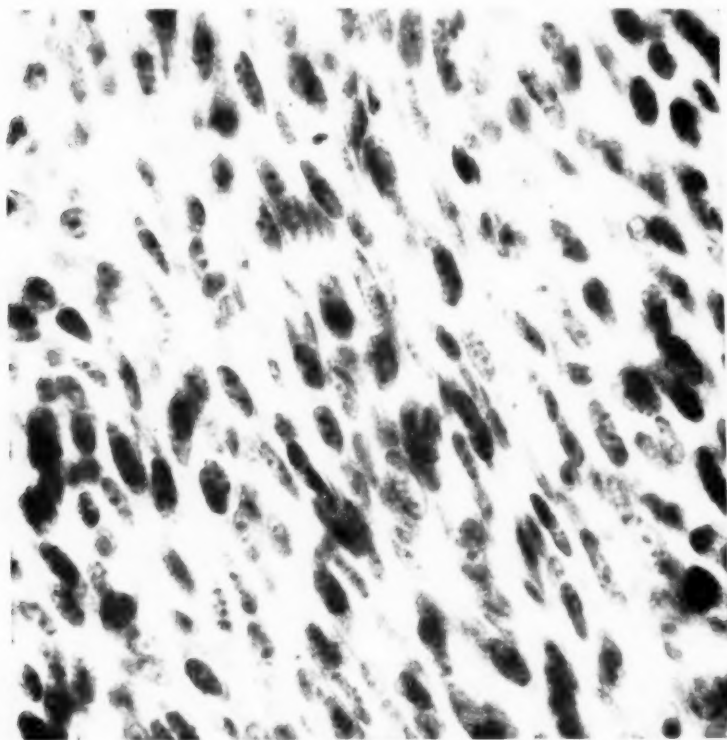
Fig. 7.—(Gyn. Path. No. 27069.)   High power view of area to the right of blocked
area in Fig. 5.   This shows rather typical spindle-shaped cells which form the pre-
dominant cell in both the biopsy and parent tumors. See Fig. 4, etc.

general shape, the familiar relation between cytoplasm and nucleus
and tinctorial properties suggestive of typical spinal cells. A distinct
cell membrane, however, was absent. From cells of this appearance
to those regarded as typical transitional cells every intermediate
gradation may be seen. In this as in previous studies all cells not
typical of the spinal- or spindle-cell varieties were classed as transi-
tional cells. In this manner the well-nigh hopeless task was avoided
of trying to classify an endless variety of cells possessing slight mor
phologic or tinctorial differences.

In comparing the histologic picture presented by biopsy material and numerous microsections of the parent tumor obtained by operation, we observed 13 (30.2 per cent of 43) instances in which the biopsy did
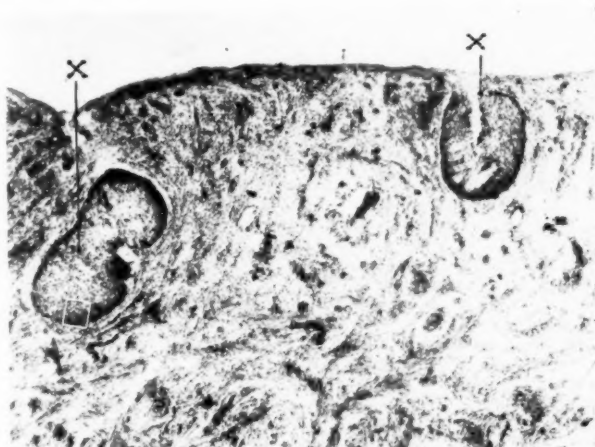
Fig. 8.—(Gyn. Path No. 27099.)   This is from the parent tumor of which Gyn. Path. No. 27069 is the biopsy.   Low power of typical cancer alveoli at X.   These are composed in most part of spindle cells.
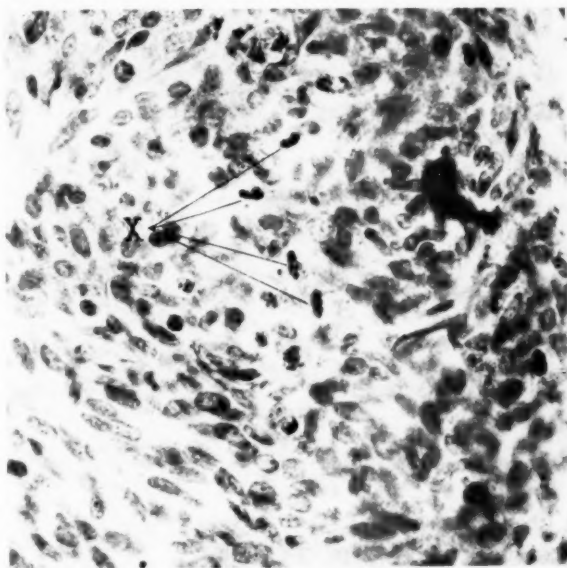
Fig. 9.—(Gyn. Path. No. 27099.)   Higher power of blocked area in Fig. 8.   This shows both round- and spindle-shaped cells and from an area as this a determination of the predominant type of cancer cell is impossible.   Mitotic figures are seen at X.

not reflect the cytomorphology of the parent tumor.   This is brought out in Table III.

From the foregoing it is evident that in 4 instances the biopsy findings clearly and erroneously indicated a tumor of the spindle-cell variety.   In 9 other instances it was impossible to distinctly define a

predominant variety of cancer cell, though in each instance the parent tumor was composed of cancer cells predominantly of the transitional-cell type.

TABLE III.   TRANSITIONAL-CELL CANCER (43 CASES)

Biopsy showing predominance of spindle cancer cells	4 specimens
Biopsy showing equal number of transitional and spindle cancer cells	5 specimens
Biopsy showing predominance of spinal cancer cells	0 specimen
Biopsy showing equal number of transitional and spinal cancer cells	4 specimens

Table III does not consider the occurrence of epithelial pearls, mitoses, giant cells, or nucleoli. These have been considered separately in order
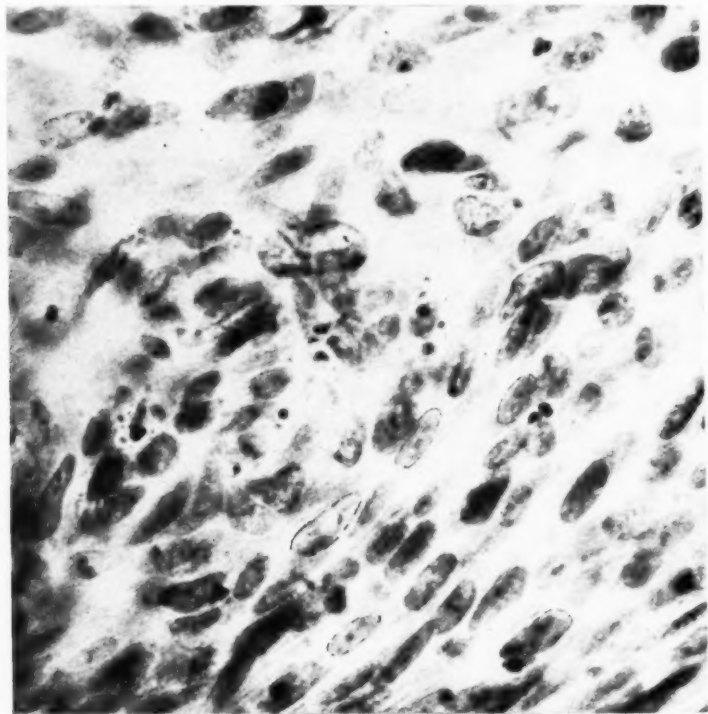
Fig. 10.—(Gyn. Path. No. 27099.)   High power from another area in cancer alveolus seen in Fig. 8.   These spindle cells form the predominant type of cancer cell in both the biopsy and parent tumors of this specimen which is classed as a spindle-cell cancer.

better to evaluate the degree of similarity existing between biopsy material and the parent tumor.

Epithelial pearls were encountered in 8 of the 43 cases of transitional-cell cancer as shown in Table IV.

TABLE IV.   SHOWING DISTRIBUTION OF EPITHELIAL PEARLS IN EIGHT CASES OF TRANSITIONAL-CELL CANCER

		NUMBER OF CASES	
Biopsy	} 4	0	1
Parent tumor		3	0

From the foregoing it is seen that in only half of the cases showing epithelial pearls did the biopsy and parent tumor correspond in this particular observation.

Mitotic figures were noted in the biopsy material and parent tumor of every specimen. As evidence of mitosis we accepted only nuclear changes characterizing the metaphase or anaphase of the karyokinetic cycle. Not infrequently the telophase could be readily identified where other mitoses were numerous but by itself we did not consider this appearance sufficiently characteristic for identification in ordinary micro
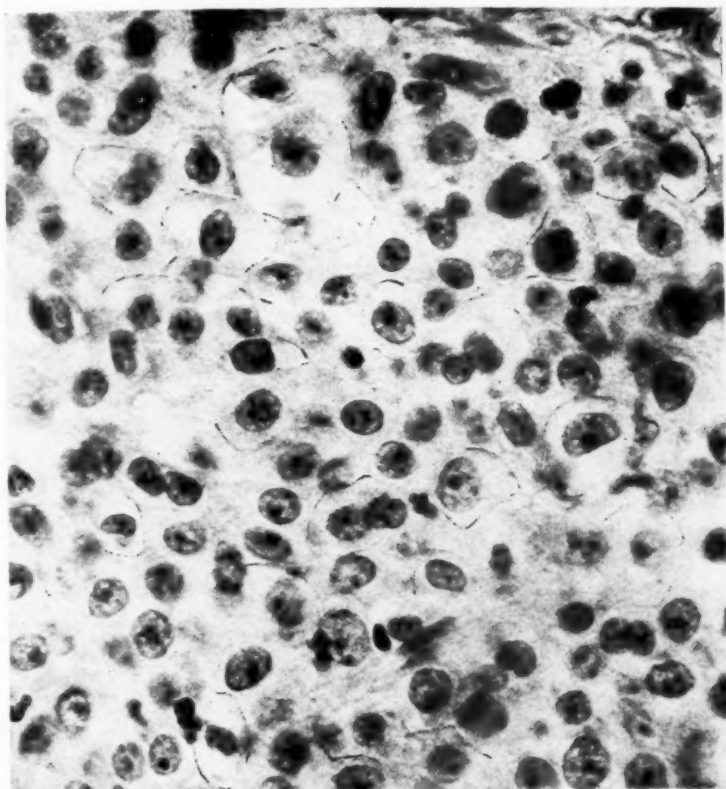
Fig. 11.—(Gyn. Path. No. 26737.)   Biopsy material showing spinal type of cancer cells.   The cell membranes do not come out well so that some retouching has been necessary.   Compare with Fig. 12.   Other areas show transitional-cell types in about equal numbers so that from the biopsy it is impossible to decide as to the predominant type of cancer cell.

sections. Possibly what we have termed the metaphase may be a stage in the prophase. However, we did not construe an irregularly rounded, pyknotic nucleus as definite evidence of mitosis obvious as this might be to the experienced observer.

Giant cells either mono- or polynuclear were observed in 25 of these 43 cases. In only 5 instances did the biopsy and parent tumor material fail to correspond in this detail.

Nucleoli were observed in all but five specimens. In two of these the absence of nucleoli occurred in both biopsy and parent tumor material while in the remaining 3 was there lack of similarity.

SPINAL-CELL CANCER

In the group of cancers where the spinal type of cancer cell predominates we have only 6 cases where biopsy material was available
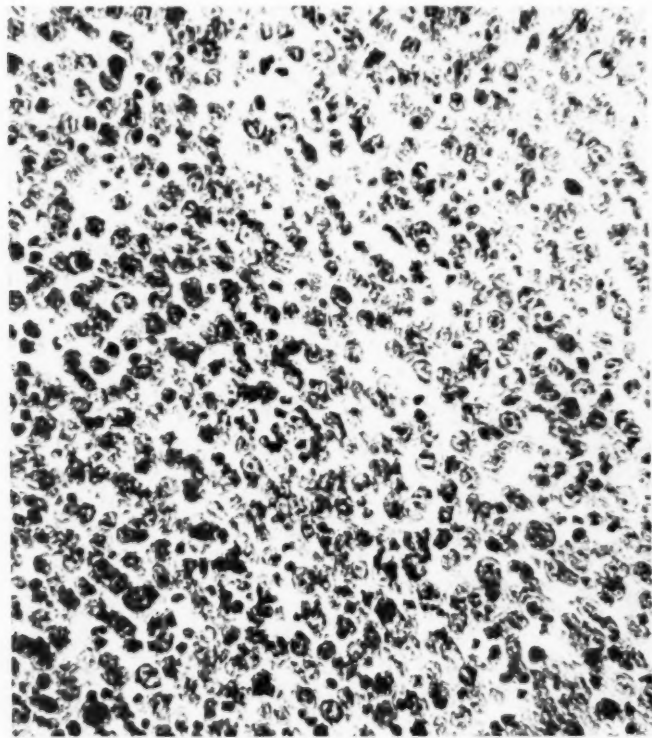
Fig. 12.—(Gyn. Path. No. 26800.) Section from parent tumor of which Fig. 11 represents the biopsy. Cells are practically all of the transitional-cell type, no definite spinal cells being seen in sections of the parent tumor.

for comparison with tissue from the parent tumor. Table V illustrates clearly the situation encountered in comparing the predominant cell types in biopsy and parent tumor material.

TABLE V. SPINAL-CELL CANCER (6 CASES)

Biopsy showing predominance of spindle cancer cells	0 specimen
Biopsy showing equal number of spinal and spindle cancer cells	0 specimen
Biopsy showing predominance of transitional cancer cells	1 specimen
Biopsy showing equal number of spinal and transitional cancer cells	2 specimens

Deductions obtained from such a small number of specimens may be manifestly erroneous. However, it is seen that in one instance the biopsy indicated incorrectly the presence of a transitional-cell cancer while in two instances a definite decision could not be made as to the predominate type of cancer cell.

Epithelial pearls were noted in 3 specimens. In one they were observed in both biopsy and parent tumor, in one in the biopsy and in the third solely in the parent tumor.
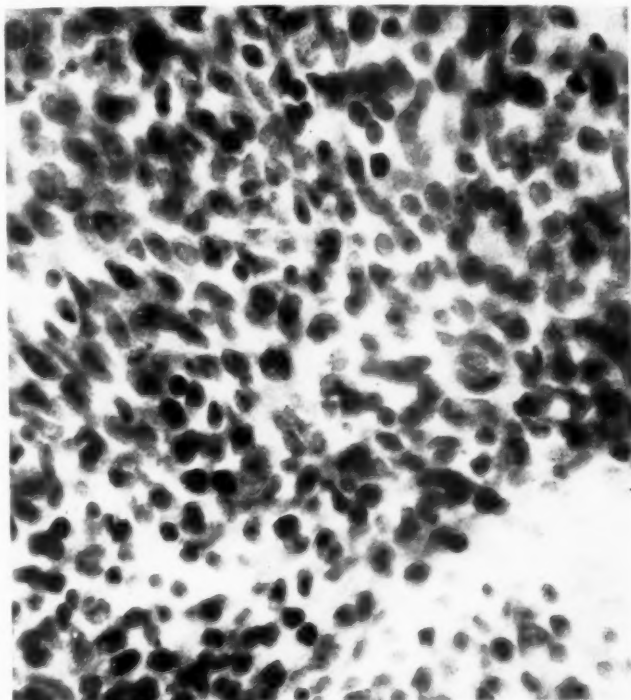
Fig. 13.—(Gyn. Path. No. 26657.)   Biopsy material showing a predominance of the transitional type of cancer cell.   Compare with Fig. 14.

Mitoses were observed in both biopsy material and the tissue from the parent tumor in every instance.

Giant cells occurred in 5 of the 6 specimens as shown in Table VI.

TABLE VI.   SHOWING DISTRIBUTION OF GIANT CELLS IN FIVE CASES OF SPINAL-CELL CANCER

	NUMBER OF CASES		
Biopsy	1	1	0
Parent tumor		0	3

Nucleoli were uniformly present in biopsy and parent tumor preparations.

SPINDLE-CELL CANCER

For this study 11 specimens were available. In Table VII are tabulated the biopsy findings in 4 specimens where though the parent tumor is predominately composed of the spindle type of cancer cell, the biopsy findings are equivocal or misleading. In the remaining 7 specimens the parent tumor confirms the biopsy.

It is seen from Table VII that in 4 specimens (36.4 per cent of 11) the biopsy material did not reflect the predominant cell type of the
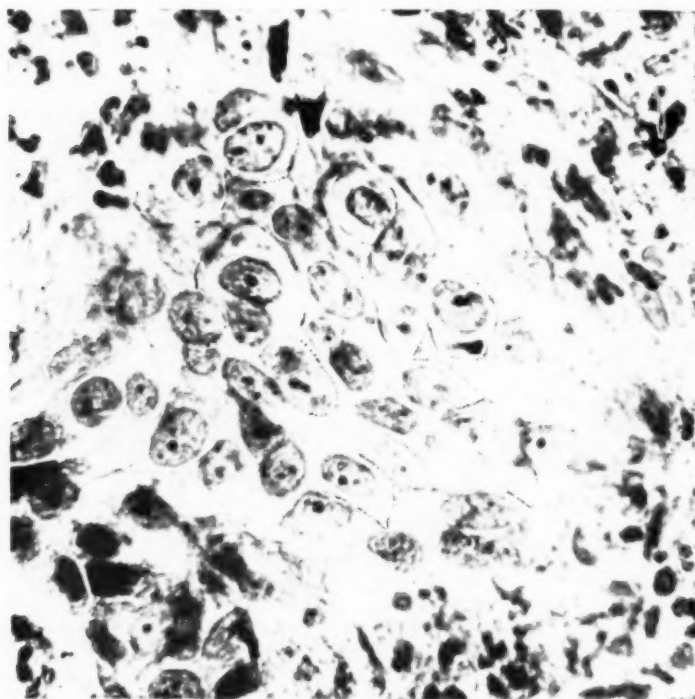
Fig. 14.—(Gyn. Path. No. 26657.)   Section of parent tumor of which Fig. 13 represents the biopsy material. This section shows a predominance of the spinal type of cancer cell which is the predominant cell type throughout the tumor.   Retouching necessary to bring out cell membranes in photograph.

parent tumor. In fact, in 3 of these specimens the biopsy indicated a pure transitional-cell type of cancer, for no spindle cells were seen in this material.

TABLE VII.   SPINDLE-CELL CANCER (11 CASES)

Biopsy showing predominance of transitional cancer cells	3 specimens
Biopsy showing equal number of spindle and transitional cancer cells	1 specimen
Biopsy showing predominance of spinal cancer cells	0 specimen
Biopsy showing equal number of spindle and spinal cancer cells	0 specimen

One other case, not included in Table VII requires mention. In this instance the biopsy revealed an overwhelming number of spindle cells while study of the parent tumor showed about an equal inci-

dence of spindle and transitional cells.   Because of the biopsy find-
ing this case was included in the spindle-cell group of cancers.

Epithelial pearls were observed in one case occurring in both the
biopsy material and the parent tumor.   The biopsy in this instance
accurately reflected the histologic appearance of the parent tumor in
all other respects.

Mitotic figures were observed in every instance in both biopsy mate-
rial and parent tumor.
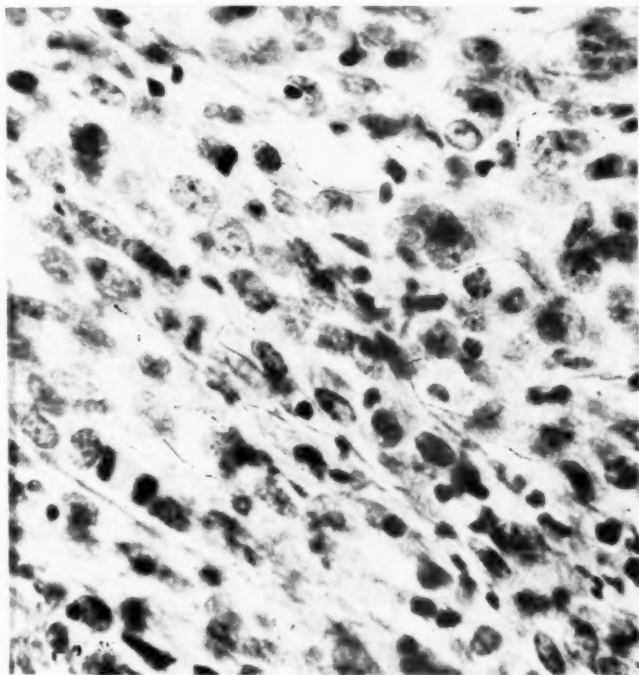
Fig. 15.—(Gyn. Path. No. 27098.)   Biopsy showing spinal type of cancer cell in pre-
dominance.   Compare with Fig. 16.

Giant cells both mono- and polynuclear were observed in 6 of these
11 specimens.   In this respect the biopsy material indicated their
presence in the parent tumor.

Nucleoli were observed in all but two biopsy specimens.   The parent
tumor in one of these showed no nucleoli while in the other specimen
they were present.

SPINAL- AND TRANSITIONAL-CELL CANCER

In this group are included 10 specimens in which spinal- and
transitional-cell types occurred in equal proportion in the parent
tumor.   It may be noted that spindle-cell types were also noted in
some of these specimens but in such small numbers as hardly to in-
fluence the histologic picture.

In Table VIII are tabulated the biopsy findings in so far as cell type is concerned in these 10 specimens.

TABLE VIII.   TRANSITIONAL AND SPINAL CANCER CELLS OCCURRING IN EQUAL NUMBERS (10 CASES)

Biopsy showing a predominance of transitional cancer cells	4 specimens
Biopsy showing equal number of spinal and transitional cancer cells	6 specimens
Biopsy showing predominance of spinal cancer cells	0 specimen

From the foregoing it is seen that the biopsy material indicated a predominance of transitional cells in 4 (40 per cent) of the 10 specimens while in the remaining 6 the biopsy findings corresponded to the parent histology.
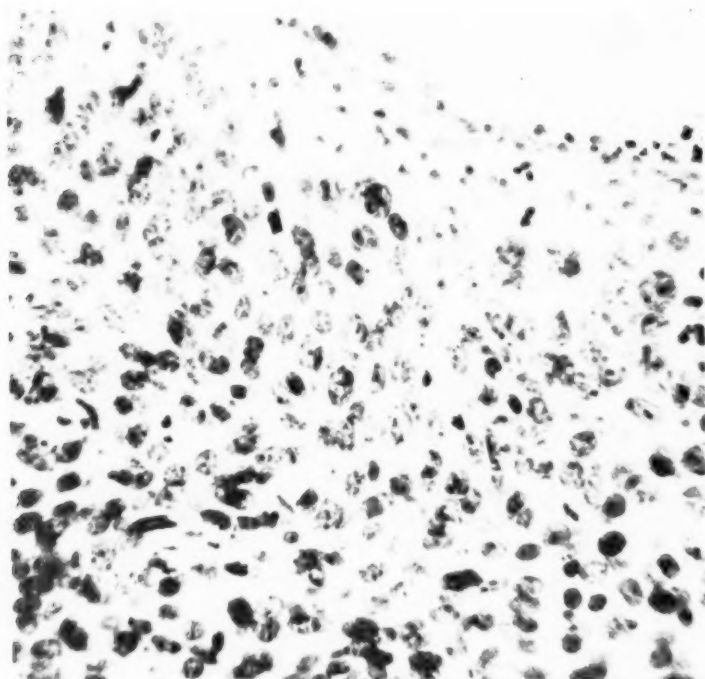
Fig. 16.—(Gyn. Path. No. 27124.)   Section of parent tumor of which Fig. 15 represents the biopsy.   The cells in this section resemble most nearly the transitional-cell type and are characteristic of the entire tumor.   A moderate number of spindle-cells are present.   (2099 mc. hours radium five days preoperatively.)

Epithelial pearls occurred in 3 specimens.   In one both biopsy material and parent tumor contained pearls while in the other two their occurrence was confined to the parent tumor, none being found in the biopsy tissue.

Mitoses and nucleoli were noted in both biopsy material and sections of the parent tumor of every specimen.

Giant cells were seen in all parent tumors and in all but two of the biopsy specimens.

SUMMARY

This study is based on 70 specimens of cancer of the cervix uteri obtained by operation at the Johns Hopkins Hospital. In each instance biopsy material was available for comparison with the histology of the parent tumor. The object of this study is to ascertain to what extent the cytomorphology of the biopsy material reflects the histologic picture of the parent tumor in so far as the predominating type of cancer cell is concerned.

In 43 specimens of *transitional-cell cancer*, study of the biopsy material revealed in 13 (30.2 per cent) instances a histologic picture that did not satisfactorily reflect the cytomorphology of the parent tumor. In 4 of these 13 specimens the biopsy material erroneously indicated a spindle-cell type of cancer and in the 9 remaining specimens it was impossible to define a predominant variety of cancer cell.

In 6 specimens of *spinal-cell cancer* it was impossible from a study of the biopsy material to definitely determine the predominant type in 3 (50 per cent). In one of these the biopsy incorrectly indicated a transitional-cell cancer.

There were 11 specimens of spindle-cell cancer available for study. In 4 of these (36.4 per cent of 11) the biopsy material did not indicate the predominant cell type of the parent tumor.

In the group of cancers where the *spinal- and trasitional-cell types* occurred in about equal proportion it was found that the biopsy material in 4 (40 per cent) of the 10 specimens available for study did not bear out the findings in the parent tumor in that they indicated a predominance of transitional cells.

Observations were made on the occurrence of epithelial pearls, mitoses, nucleoli and giant cells in both biopsy and parent tumor material.

CONCLUSION

From the foregoing observations it is permissible to conclude that in carcinoma of the cervix uteri, a study of biopsy material will, in about one-third of the material studied, fail to indicate correctly the predominate variety of cancer cell in the parent tumor.

Therefore, any studies having biopsy material as their sole basis that attempt to offer a prognosis based on the predominant type of cancer cell in cancer of the cervix uteri, face the problem of inaccuracy as stated in the preceding paragraph.

To Doctor Cullen are due my appreciation and thanks for his ever ready interest, helpful criticism, and the privilege of making this as well as previous studies.

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END-RESULTS OF THE TREATMENT OF CERVICAL CANCER BY RADIATION THERAPY

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(From the Memorial Hospital)

RECENTLY, in reviewing the cases of carcinoma of the cervix which had been accepted for treatment in 1922 and 1923 on the gynecologic service at the Memorial Hospital, an effort was made to group the cases not only from the standpoint of clinical stage of the disease present when first seen but also from the histologic standpoint of degree of anaplasia in the biopsy specimens obtained from the tumors.

Certain conclusions were reached from this study which it seemed worth while to present for consideration.

Before taking up this part of our subject, I would like to make a report on the present status of the cases treated by Dr. Harold Bailey at the Memorial Hospital previous to December 31, 1921.

TABLE I.   CASES TREATED BY RADIUM THERAPY, 1918 TO 1921 INCLUSIVE, SERVICE OF DR. HAROLD BAILEY

CERVIX	TOTAL	APRIL 1, 1928	PER CENT ALIVE 6-9 YEARS
Early	35	9	25.7
Borderline	52	7	13.4
Advanced	288	16	5.5
Recurrent	139	16	11.5

We have included no cases treated before January 1, 1918, as only small amounts of radium were available, no definite plan of treatment was being followed, and the work was really in an experimental stage. By 1918 a definite plan was established, consisting of crossfiring the lesion with vaginal and cervical applicators, bare seeds imbedded in the lesion, and radium block applied in six positions about the pelvic girdle.   Radium alone was used in all these treatments.

A review of these figures would indicate that early diagnosis still remains the most important factor in the ultimate prognosis.

Is it fair to assume that all these patients will remain free from a return of their disease?   I think not.   We have now under treatment

one of Bailey's 1919 patients who remained symptom free for eight years, then began to complain of "rheumatism" in the left leg. Examination reveals hard, nodular, metastatic masses in the left parametrium, and in the retroperitoneal lymphatic glands, anterior to the sacrum. Skiagraph of the pelvis shows cancerous invasion of the left ilium, inner wall on either side of the brim of the true pelvis, extending down into the acetabulum and well up into the body of the ilium.

Several other patients remained well for five or more years before disappearing from our records, and they are counted as dead. Of course many of these patients are advanced in years and could readily be carried away by other diseases so that we must expect a normal loss from this source. In our experience it is quite unusual to find a late recurrence in the cervix at the original site of the disease.

Such recurrences are usually in the distant parametrial and iliac lymph glands. Their presence is indicated by deep-seated obscure pain long before any gross lesion can be identified. One of the most obscure cases of recurrence I have had was associated with persistent deep-seated pain to the left of the spine midway between the umbilicus and the left costal margin. The pain became so intense that it required hypodermic medication and was present for a year before a tumor mass could be recognized. In the meantime careful roentgenographic studies had been made of the ribs, spine and pelvis, of the kidneys, gall bladder, stomach, and intestines to no avail.

My personal reaction to such a situation is that exploratory celiotomy is justified after the usual precautions to avoid an error in diagnosis. It may be quite possible to locate the metastatic lesion and to infiltrate it with gold seeds to the benefit of the patient.

In 1922 and 1923 there were 224 cases of carcinoma of the cervix admitted for treatment.

We first grouped the cases according to the clinical stage of the disease and the number of cases still alive.

TABLE II. EFFECT OF CLINICAL STAGE UPON PROGNOSIS

CLINICAL STAGE	NO. OF CASES	ALIVE	PER CENT ALIVE
Early	28	17	60
Borderline	35	13	37
Advanced	161	37	23

It is evident from Table II that early diagnosis is a most important factor in prognosis.

The slides of all the cases were then carefully studied from the histologic standpoint by Dr. Max Cutler, with the advice and cooperation of Dr. James Ewing. Twenty-four of the cases were eliminated because of unsatisfactory slides for study or grading, leaving 200 cases that seemed to fulfill all the histologic requirements.

Throughout 1926 to 1927 all biopsy specimens from cervix cases, in so far as it was possible to do so had been not only described from the histologic standpoint but had been divided into Grades I, II, III, corresponding in a general way with Broder's Grades i, ii, iii, iv.

A certain facility and expertness had therefore been acquired in identifying these different grades which was of great help in studying the 200 cases of the 1922-1923 series.

The general principle followed in grading the tumors was that of the degree of anaplasia present in the cells including also the relative amount of stroma present. Ewing's histologic criteria indicative of anaplasia are cellular overgrowth, atypical qualities of cells, variation in size, shape, and staining qualities of nuclei, infiltration tendencies, loss of polarity, number and atypical quality of mitoses and absence of adult differentiated characteristics.

Just as had previously been recognized by Broders, Martzloff, Schottlaender and Kermauner, et al., it was found that three large groups could be readily established, each fairly distinct from the other.

Group A made up of a small group of cases characterized by cells adult in character, highly differentiated, with a tendency to hornification and pearl formation; this we called the adult type Grade I. At the other extreme there was also a small group, Group C, in which the cells were small and round or spindle shaped, the nucleus markedly hyperchromatic with numerous atypical mitoses. The cells showed absence of squamous character, atypical qualities, complete loss of differentiation, and diffuse infiltrative growth. This was called anaplastic type Grade III.

Between these two extremes there is a larger intermediate group, Group B, showing only partial differentiation and moderate anaplasia. In this group squamous characters are either slight or more often absent. The growth may be atypical but lacks diffuse infiltration, there is a partial loss of polarity. These cells are large and frequently show plexiform arrangement. This we called plexiform type Grade II.

It is, of course, impossible to draw a sharp line of distinction between the three histologic groups. In a small proportion of cases it has been somewhat difficult to decide whether a tumor belonged to the plexiform or anaplastic group. Tumors presenting this structure, however, are distinctly radio sensitive and consequently are classified as anaplastic.

The differentiation between the adult and anaplastic forms has presented no difficulties and the presence or absence of squamous characters has served as a good basis for division between the adult and plexiform types. It should also be realized and borne in mind that we have been very greatly aided in establishing the classification of individual tumors by our knowledge of the probable behavior of the cells in the tumor under consideration to radiation, in addition to a consideration of the histologic criteria referred to. From time to

time, therefore, a tumor has been recognized from its cellular structure as radio sensitive and, although of plexiform type, has been placed in Group iii anaplastic.

One of the important determining elements in influencing us toward anaplasia as a basis for our classification is the fact that we are dealing with end-results based entirely on radiation therapy and for a long time it has been recognized by many writers that the higher the degree of differentiation of the tumor cells, the lower the potential malignancy and the greater the radio resistance of the cells.

Conversely the greater the degree of anaplasia with infiltrative tendencies and loss of differentiation the greater the degree of malignancy and also the degree of radio sensitivity.

Table III shows the relative frequency of the different histologic grades as compared with Martzloff's classification.

TABLE III.   SHOWING INCIDENCE OF STRUCTURAL TYPES AS COMPARED WITH
MARTZLOFF'S THREE GROUPS

| WRITER'S CLASSIFICATION | | | MARTZLOFF'S CLASSIFICATION | | |
CELL TYPE	NO. CASES	PER CENT	CELL TYPE	NO. CASES	PER CENT
Adult (i)	35	17	Spinal	30	22
Plexiform (ii)	123	62	Transitional	90	66
Anaplastic (iii)	42	21	Spindle	17	12

As indicated in Table III, the majority of the tumors belong to the intermediate or plexiform group, whereas the smaller groups comprise the adult and anaplastic types of cells. Forty-two out of two hundred cases, or 21 per cent, belong to the highly undifferentiated anaplastic cell type. It is significant that one in five cases of this series is a very cellular, malignant, and anaplastic tumor and consequently highly susceptible to radiation.

A study was made of twenty early and borderline cases which had died despite treatment.

TABLE IV.   SHOWING DISTRIBUTION OF STRUCTURAL TYPES AMONG TWENTY FAILURES
IN THE CLINICALLY EARLY AND BORDERLINE GROUPS

CELL TYPE	NO. CASES	PERCENTAGE IN 20 EARLY AND BORDERLINE FAILURES	PERCENTAGE IN TOTAL SERIES
Adult	5	25	17
Plexiform	12	60	62
Anaplastic	3	15	21

Table IV fails to show any definite relationship between cell type and result, despite the fact that there was no variation in treatment. This emphasizes the need for recognition of other factors which influence end-results.

A study was made of the cell type in 30 cases of advanced carcinoma of the cervix which had remained well four and five years.

TABLE V. SHOWING THE DISTRIBUTION OF STRUCTURAL TYPE AMONG 30 CASES OF
ADVANCED CARCINOMA OF THE CERVIX WELL FOUR AND FIVE YEARS

CELL TYPE	NUMBER OF CASES
Adult	1
Plexiform	15
Anaplastic	14

The result of this study was quite unexpected. It would seem, however, to suggest that the prognosis in the clinically advanced group of cases under adequate radiation therapy is much better, the more cellular and malignant the cell type, as this cell type is decidedly radio sensitive.

It must be borne in mind that these patients all received very thorough irradiation with radium and x-ray.

In order to have a correct basis for comparing the percentage of cures in relation to the clinical stage of the disease and the histologic type under radiation and surgical treatment, respectively, we have grouped our early and borderline cases in each histologic grade together, representing the probably operable cases and the advanced cases in each histologic grade as corresponding to the probably inoperable surgical group and have obtained Table VI.

TABLE VI. SHOWING PERCENTAGE OF CURES IN RELATION TO THE CLINICAL STAGE
OF THE DISEASE AND THE HISTOLOGIC TYPE UNDER RADIATION AND
SURGICAL TREATMENT, RESPECTIVELY

	RADIATION				SURGERY	
CELL TYPE	STAGE OF DISEASE	TOTAL NO. CASES	NO. WELL	PER CENT CURED	PER CENT OF OPERATIVE CURES, J. H. H., MARTZLOFF	PER CENT OF OPERATIVE CURES, MAYO CLINIC, BRODERS
Adult (Grade I)	Early and Borderline	10	5	50	47	53
	Advanced	25	1	4		
Plexiform (Grade II)	Early and Borderline	21	9	43	24	21
	Advanced	102	15	14		
Anaplastic (Grade III)	Early and Borderline	9	6	66	9½	9½
	Advanced	33	14	42		

Examination of Table VI verifies again the importance of early diagnosis as a prognostic factor regardless of cell type.

Table VII shows the relation between prognosis and histologic grade in advanced cases of carcinoma of the cervix treated by radiation.

TABLE VII. SHOWING RELATION BETWEEN PROGNOSIS AND STRUCTURAL TYPE IN
ADVANCED CASES OF CARCINOMA OF THE CERVIX TREATED BY RADIATION

CELL TYPE	NO. CASES	CASES WELL	PER CENT CURED
Adult (I)	25	1	4
Plexiform (II)	102	15	14
Anaplastic (III)	33	14	42

From these figures it would seem that the prognosis in advanced cancer of the cervix under radiation therapy is extremely poor in the adult cell type, Grade I, and unexpectedly favorable in the anaplastic type, Grade III.

The conclusion seems justified that in the advanced stage of the disease the prognosis improves with the degree of anaplasia under radiation therapy.

A study of surgical end-results in the treatment of carcinoma of the cervix indicates that the degree of malignancy of the cell type in the individual tumor is a most important controlling factor. The best results are obtained in the highly differentiated adult cell group and the worst in the very cellular infiltrating malignant cell type.

TABLE VIII. PERCENTAGE INCIDENCE OF FIVE-YEAR CURES FOR THE DIFFERENT TYPES OF EPIDERMOID CARCINOMA OF THE CERVIX UTERI

	SPINAL CELL CANCER GRADE II OF BRODERS	TRANSITIONAL CELL CANCER GRADE III OF BRODERS	SPINDLE CELL CANCER GRADE IV OF BRODERS
The Johns Hopkins Hospital (Martzloff) (Surgery)	47%	24%	9½%
The Mayo Clinic (Broders) (Surgery)	53%	21%	9½%
Memorial Hospital (Radiation)	50%	43%	42-66%

CONCLUSIONS

1. Epidermoid carcinoma of the cervix may be classified histologically into three grades, based primarily upon the degree of anaplasia. These groups correspond closely to three degrees of potential malignancy as well as to three grades of radiosensitivity (low, medium and high).

2. The adult type of carcinoma of the cervix (Grade I) is markedly resistant to radiation; the anaplastic type (Grade III) is highly radiosensitive, whereas the plexiform type (Grade II) occupies an intermediate position.

3. The factors which determine prognosis in carcinoma of the cervix, as in other diseases, are multiple and not single. The clinical stage of the disease at which treatment is instituted and the radiosensitivity of the tumor are believed to be the most important factors in prognosis when radiation is employed.

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WHAT CAN WE LEARN FROM A STUDY OF MORTALITIES?

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WE ALL like to report successes, but it is from failures that we learn our shortcomings and the lessons which should be indelibly impressed upon our memories.

A surgical audit is a necessity in every clinic, otherwise, owing to the fact that our successes far out-number our failures, we forget the latter and go complacently along self-satisfied.

At the Long Island College Hospital our organization is such that the major part of the gynecologic and obstetric surgery is done by the junior staff and senior resident. Hence it is imperative that we have a critical review in order that merit may be rewarded and carelessness corrected.

Like general surgery, gynecologic surgery is divided into imperative and elective groups. In the imperative group will fall the tragic ectopics, uterine and other visceral ruptures, torsions and acute suppurative conditions requiring immediate drainage. It is, however, with the elective group that this analysis chiefly has to do.

The woman about to undergo an elective operation for pelvic lesion has a right to be safeguarded from infection, morbidity, and death.

These women are frequently poor surgical risks, for many are overworked, underfed and have struggled along for years with handicapping pelvic lesions which have upset the digestion, drained the tissue fluids, disturbed body metabolism and endocrine balance, lowered the hemic content or impaired the myocardium. Were it not for these coexisting conditions the mortality in gynecology would, with malignancy excluded, be lower than that of a general surgical service, for we are dealing with patients who have an operation on advice, not as an immediate necessity.

In order to safeguard these women, the routine procedure in our department for years has been to require the following minimum preoperative requisites, before all elective sections, namely:

1. A complete history and general physical examination.
2. A leucocyte count of between seven and ten thousand.
3. A polymorphonuclear percentage of from 65 to 80.
4. A hemoglobin of at least 60 per cent.
5. A sedimentation time of ninety minutes or more.
6. A normal urinalysis, and an adequate kidney function.
7. A temperature of 98.6° F. for at least forty-eight hours before operation.
8. A systolic blood pressure between 110 and 150.

9. A negative Wassermann, and finally, that all elective preoperatives have rest in bed *in the hospital* for a period of at least forty-eight hours, during which time the intake of fluids, water, milk, etc., must be at least two and one-half quarts *per diem*, while the usual sugar intake of the individual must be at least quadrupled.

Without making any attempt to draw conclusions, except to discover defects, we have analyzed our mortality for the past five years. During this period 4,270 women have been admitted to the gynecologic wards and of these 1,145 were not operated upon, while 3,125 had either pelvic or abdominal operations or both. The total mortality among 4,270 admissions was 138; 43 of these were nonoperative deaths, therefore need not be considered in this analysis. In the 3,125 patients operated upon, there were 95 deaths. Each of the fatal cases has been studied with reference to the preoperative status, the type of operative procedure and the postoperative course. As we have proceeded with the consideration of the deaths in the elective group, it has been illuminating to note that the fatal issue can be attributed to one of the following causes: Some omission or misinterpretation of the history, physical or laboratory findings or (a) important preoperative requisites that make for a good operative risk have many times been disregarded; (b) or the employment of the high Trendelenburg posture, in combination with high blood pressure, has produced cardiac embarrassment, while prolonged Trendelenburg, in patients with low blood pressure, has increased the occurrence of shock; (c) or too much surgery has been done at one sitting; (d) or the time consumed in operating has frequently overreached the maximum of safety; (e) or forty-eight hours of rest in bed, in the hospital, which is so imperative, has been disregarded; (f) or patients have been operated upon who have been the subject of prolonged subacute or chronic infection, with a leucocytosis or a low white cell count, a low polynuclear percentage or a low platelet count, show a poor reaction to any operative procedure, or the introduction of added infection; (g) we have also learned that a low grade temperature of 99.2° F. plus means infection, and operation in such cases should be postponed until the temperature is normal and has remained normal for several days; (h) that operation in most skilled hands, in the presence of an active infection is not only dangerous, but should be limited to simple incision and drainage, and finally that the routine removal of the appendix adds to the morbidity and often to the mortality.

Upon further analysis we find that in the 1,470 laparotomies there were 607 double cases (vaginal and abdominal work done at the same sitting, under one anesthesia). In addition there were 1,529 vaginal operations, not including the 607 above mentioned.

The gross operative mortality for the five years was 2.9 per cent. This we have divided into:

1. *Malignancies,* where the abdomen was opened to confirm a diagnosis and an inoperable condition found. There were 23 of such patients who died from two weeks to ten weeks after operation, during their period of hospitalization.

2. *Emergency Deaths.*—In this group are included 20 patients, 3 tragic ectopics; 3 acute appendices with diffuse peritonitis; 11 cases of pelvic abscess which were drained after periods of prolonged sepsis; 2 gall bladders, and 1 ruptured ovarian cyst.

3. In the *elective group* there were 52 fatalities; 2 of these were vaginal operations, one dying from an intercurrent pneumonia two weeks following operation, and the other from acute suppurative peritonitis, following the use of radium. These will not be considered further in this report.

In the analysis of the preoperative status of the 50 fatal abdominal sections, the following facts are significant: period of preoperative hospitalization, 12 of these had less than twenty-four hours of observation and preoperative preparation; 17 less than forty-eight hours; only 21 had more than forty-eight hours of hospitalization. It is at once apparent that three-fifths of these cases were operated contrary to the regulations laid down in our preoperative routine. It has been our experience that many patients are operated too soon after their admission. A woman who is about to undergo a major operation needs considerable time in the hospital to recuperate from the nervous and physical exhaustion which the preparation in arranging home conditions too often entails. Furthermore, it is not possible in a time less than forty-eight hours to complete the preoperative study of her urine, blood pressure, blood sedimentation time, blood chemistry, Wassermann, and the other clinical and laboratory findings which are so essential to success.

Blood Studies.—In these 50 deaths following elective sections, 15 cases had a leucocyte count of above 10,000; 14 a count of less than 7,000 and 21 a count of between 7,000 and 10,000. Here again it is apparent that three-fifths of the cases showed leucocytic evidence of either latent infection or a leucopenia suggestive of low resistance reserve.

In the further study of the blood of these patients, taking 65 to 80 per cent to be the normal limits of polymorphonuclear percentage, we find that 6 cases had a polynuclear count of above 80 per cent; 16 had a count of less than 65 per cent, while 5 had both a white count above 10,000 and a polynuclear count of above 80, and another 5 had both a white count of under 7,000 and a polynuclear count below 65.

This analysis shows that among 50 deaths there were 41 patients who had something abnormal in their preoperative blood or differential count, and should have had further preoperative study before being subjected to operation.

There was only 1 patient in this elective group who was operated with a hemoglobin of under 60 per cent, for it has been our custom to transfuse all patients when the reading is below this standard. During the past three years the blood sedimentation time has been included into the preoperative routine and no patient is subjected to an elective procedure unless it be a simple incision and drainage of an abscess, unless the blood sedimentation time is ninety minutes or more. For, in our experience of over 3,500 readings, we have found that the rapid settling of the red cells is the most sensitive laboratory test to the presence of infection, and even in the absence of leucocytosis and elevation of temperature, a rapid blood sedimentation time indicates subacute or latent chronic infection.

By carefully observing this we have been able to eliminate the lighting up by operation of quiescent infection.

Blood Pressure has a signal significance on the prognosis of operative patients. A systolic reading of 110 to 150 may be considered as within the normal range in patients below the age of fifty-five. In this series, 8 had a systolic pressure of less than 110; 11 above 150; only 2 were classed as hypertension, having pressures of 185 and 214 respectively. Ether, gas, and ethylene all increase systolic pressure for a certain period during the administration of the anesthesia; prolonged anesthesia, however, associated with tissue trauma and blood loss, always lowers pressure.

The Trendelenburg posture temporarily increases systolic pressure and adds to cardiac embarrassment or in the presence of hypotension, contributes to surgical shock.

Anesthesia also has its effect upon the renal function. In this analysis there were 6 patients who had a glycosuria; 14 with more than a faint trace of albumin; 1 had casts without albuminuria; 4 had acetonuria without glycosuria; 2 had pus in the urine, and 4 were diabetics. From this it is evident that 31 of the 50 had some chemical or microscopic change in the preoperative urine which necessarily increased the operative risk, and probably contributed its part in the final tragedy. Furthermore, the kidney function as demonstrated by the phenolsulphonephthalein test and the concentration estimation, are important preoperative essentials. Study of these records shows that little reliability can be placed upon the former, unless the drug is administered intravenously and, notwithstanding the fact that all but four had an estimated phthalein of over 40 per cent, the postoperative records indicate kidney inefficiency.

Low grade temperature prior to operation has a greater significance than has generally been attributed to it. Twenty-eight of our patients had a temperature of 99° or more during the twenty-four hours prior to operation; then, in the light of this study, all of these 28 should

have had their operations postponed, for operative trauma excites a reaction in these quiescent low grade infections.

In determining the type of operation for a particular case, one is frequently confronted with a multiplicity of lesions. For example, in prolapse we commonly have to deal with a cystocele, enterocele, infravaginal hypertrophy of a lacerated cervix, subinvolution and backward displacement of the enlarged uterus. The correction and cure of this pathology requires a series of plastics, all of which are time-consuming, and not infrequently upon opening the abdomen to complete the operation by shortening the round and uterosacral ligaments, the surgeon is confronted with the problem of what to do with the appendix. Many times there has been a history of a chronic or subacute appendicular involvement, or on inspection the appendix is kinked, held down by adhesions, or contains concretions, all of which may be accepted indications for its removal, yet experience teaches us that the prognosis is definitely influenced by this routine procedure.

To illustrate this fact we have studied the charts of 100 patients on whom we did a hysterectomy for fibromyomas of the uterus without coexisting infection; in 50 of these the appendix was removed, while in the second group of 50, the appendix was not disturbed.

Morbidity	WITH APPENDECTOMY	WITHOUT APPENDECTOMY
Average number days with temp. above 100.4°	3.0	2.3
Wound infections	5.0	0.0
Stitch abscesses	3.0	0.0
Pelvic abscess	1.0	0.0
Local peritonitis	1.0	0.0

In the fatalities among the 50 elective sections, the appendix was removed 17 times, 15 of these as routine, or by request. In the laparotomies which were done to supplement plastic procedures for birth injuries and displacements, 6 appendices were removed; in connection with hysterectomy 8 times and in the course of other abdominal operations 3 times. Therefore, in 17 of our fatal sections, the appendix was removed. Hence we must admit ·that, based on these figures, multiplicity of operations and incidental appendectomy contributed largely to the unsatisfactory results recorded in this series.

Another factor which makes for the success or failure in an operation is the time consumed in operating. The average operating time in this group of 50 was seventy-six minutes; less than sixty minutes were consumed in 18 and more than sixty minutes in 32. It is therefore evident that three-fifths of these patients had a longer period of anesthesia than can be considered as the safe maximum.

The indications for operation according to postoperative diagnosis were as follows:

Fibroids, uncomplicated	9
Fibroids and infection	5
Adenomyoma	2
Adenomyoma and infection	1
Fibrosis uteri and endocervicitis	1
Perimetritis, subacute salpingitis	3
Acute salpingitis	2
Tuberculous salpingitis	4
Postpartum infection (multiple thrombophlebitis)	1
Bilateral dermoid and infection	1
Inflammatory tumor of sigmoid	1
Lacerations and retroversion	2
Lacerations and small fibroid	1
Lacerations and chronic appendicitis	1
Lacerations, endocervicitis and prolapse	2
Lacerations and cholelithiasis	1
Nontragic ectopic	2
Nontragic ectopic and hydrosalpinx	1
Serous cyst, adenoma, bilateral	1
Subacute salpingitis, pyosalpinx	1
Acute salpingitis, ovarian cyst	1
Mitral stenosis (sterilization)	1
Fibroid and peritonitis	1
Subacute peritonitis	1
Subacute cholecystitis and subacute appendicitis	1
Cholangitis	1
Subacute cholecystitis	1

Study of the foregoing list of pathologic indications throws little light upon the end-results, except that among these fatalities, birth injuries or their sequelae were the predominating lesion in seven instances, yet other operations requiring the invasion of the peritoneal cavity were performed. Combination operations done on the pelvic structures and upon the viscera of the upper abdomen at the same time cannot be accepted as sound surgical judgment, and are in violation of accepted surgical principles; we have had 2 deaths which may be attributed to this cause.

Operation in the acute or subacute stage of adnexal infection is still a debatable question among many operators; however, in this clinic we seldom operate while the lesion is "hot," except to incise and drain a pelvic or appendicular abscess; yet, in this analysis we find 6 deaths which can be directly attributed to bad judgment in not accepting the evidence of a rapid blood sedimentation time and other blood findings indicative of pus.

Nature establishes protective barriers in every infection; manipulation and dissection break these down and spread the infection; "pus is pus" and should be drained and not spread. Too often the operator opens the abdomen on a faulty diagnosis and finds purulent foci and has not the courage or the judgment to back out and drain, but attempts extirpation in friable tissues, disseminating the infection.

We next come to the consideration of the question, from what did these patients die? The cause of death as recorded on the hospital

record is too often incorrectly stated as myocardial failure. Only 8 cases of 29 so classified can be accepted as true circulatory failures. For a detailed study of the postoperative course points to infection and peritonitis. Twenty-one have been reclassified at Staff Conference or at autopsy as fulminating infection or peritonitis.

It is further interesting to note that of this number only one of the 8 had definite cardiac symptoms prior to her operation, yet among more than 300 patients operated for abdominal lesions who recovered, there were many who had murmurs or symptoms of cardiac distress.

We have come to the conclusion that a preoperative case which has a definite history of a cardiac load has a better chance for an operative recovery than many of these women who are admitted and go to operation with no signs of heart lesion, for in the former greater care is taken in their preparation, their anesthesia is more carefully selected and less surgery is done, or, if an extensive procedure is necessary, it is done at several sittings. The other seven cases included two pulmonary emboli, one coronary thrombosis and four cardiac failures. In three of the latter, high blood pressure in conjunction with the Trendelenberg posture and prolonged anesthesia resulted in death within eighteen hours after operation; all three were difficult to anesthetize, being of the obese, short-necked type, their ages ranging from forty to sixty-two years. The fourth case was an opium addict, dying of postoperative exhaustion.

Surgical accidents and complications are often unavoidable and certainly are not preventable. Table I is illustrative of this group.

TABLE I.   POSTOPERATIVE COMPLICATIONS—SURGICAL ACCIDENTS

DIAGNOSIS	OPERATION	CAUSE OF DEATH	
1. Lacerations, Retroversion	Plastics, Laparotomy	Lobar Pneumonia	6 da.
2. Fibroids, Salpingitis	Hysterectomy Plus	Bronchopneumonia	7 da.
3. Ectopic	Colpotomy, Salpingitis	Lobar Pneumonia	4 da.
4. Lacerations, Fibroid	Plastics, Radium, Lap.	Parotitis-Pneumonia	21 da.
5. Adenomyoma	Hysterectomy	Urinary Suppuration	2 da.
6. Fibroids	Hysterectomy Plus	Wound Rupture	70 da.
7. Subacute Appendicitis	Appendectomy, Susp.	Wound Rupture	20 da.
8. Cholangitis	Cholecystotomy	Wound Hemorrhage	28 da.

Comment

1. 7,150—Poly. 61—Temp. 99.2°—Operation 100 Min.—Interval Appendectomy.
2. 6,600—Poly. 78—Operation 70 Min.—Appendectomy.
3. 10,600—Poly. 76—2 Per Cent Sugar—Operation 55 Min.—Colpotomy and Curettage—Wassermann 4+.
4. 11,200—Poly. 65—B. P. 112/76—Operation 75 Min.—Appendectomy.
5. B.P. 18/100 F. T.—Albumin—Ureter Cut.
6. 11,800—Poly. 70—Temp. 99°—Interval Appendectomy—Sutures Removed Eighth Day—Previous Cardiac.
7. 7,800—Poly. 64—Should Not Have Been Operated (Surgeon) Wound Opened Seventh Day.
8. 6,400—Poly. 64—Intense Jaundice 2½ Months—Wound Hemorrhage—Peritonitis.

TABLE II. CIRCULATORY GROUP

DIAGNOSIS	OPERATION	TIME	W.B.C.	PMN.	PRE-OP. T.	URINE
1. Cyst, Salpingitis	Salp. Oophorectomy	35M.	15,600	86	100.6°	Alb.
2. Ectopic, Hydrosalpinx	Perin., B. S. & O. Susp.	60M.	9,900	72	99.0°	Neg.
3. Adenomyoma, Salp. Oophoritis	Hyst., B. S. & O. App.	70M.	7,400	74	Norm.	Neg.
4. Ectopic	Curettage, S. O.	70M.	4,300	60	99.0°	Neg.

Comment

1. Ovarian Cyst Ruptured Twelve Hours Before, Acute Salpingitis—Cardiac?
2. Rectal Injury in Doing Perineorrhaphy—Septicemia.
3. Following Day Chills. Profound Toxemia—Cardiac?
4. Cardiac Death?

TABLE III. CIRCULATORY GROUP

DIAGNOSIS	OPERATION	TIME	W.B.C	PMN.	B. P.	PRE-OP.T.	DIED HR.
1. Perimetritis, Salp. Oophoritis	Plast., Hyst., B. S. O.	170M.	8,200	56	152/90	N.	39
2. T.B.C. Salpingitis	Hyst., B. S. O.	100M.	9,400	57	110/70	N.	43
3. Sigmoid Ulcer, S. Oophoritis	Hyst., B. S. O., Colost.	105M.	11,000	77	115/65	N.	66
4. Subacute Cholecystitis	Cholecystectomy	55M.	6,400	57	90/60	99.2	55

Comment

1. Treated Diabetic—Double Operation—Delayed Shock.
2. Profound Shock—Slow Weak Pulse—Cardiac Collapse.
3. Albumin in the Urine—Temperature 104°—In 13 Hr. Cardionephritic.
4. Jaundice 2 Mo.—Delayed Shock—Cardiac Failure.

TABLE IV. CIRCULATORY GROUP

DIAGNOSIS	OP. TIME	B. P.	W.B.C.	P.M.N.	PRE-OP. TIME	URINE
1. Fibroid, Necrosis, Hydrosalpinx	100 M.	120/74	6,800	69	99.4°	Alb.
2. Salp. Oophoritis, Perimetritis	85 M.	86/70	8,800	71	Norm.	Neg.
3. Fibroid Uterus	75 M.	97/58	5,900	68	99.2°	Neg.
4. Fibrosis Uterus	105 M.	160/102	8,200	73	Norm.	Neg.

Comment

1-2-3. Supracervical Hysterectomy, Bilateral Salpingo-oophorectomy.
4. Panhysterectomy.
1-2. Severe Shock—3 None—4 Mild—600 c.c. Blood Loss.

TABLE V. PERITONITIS

DIAGNOSIS	OPERATION	TIME	B.P.	W.B.C.	PMN.	DIED
1. Fibroids	Hysterectomy	90 M.	162/100	12,200	85	3 Da.
2. Fibroids, Infection	Panhysterectomy	115 M.	164/ 84	9,800	68	5 Da.
3. Serous Cyst, Bilat.	Bilat. S.O., Susp., App.	60 M.	112/ 72	6,600	68	4 Da.
4. Fibroid	Mymoectomy	60 M.	114/ 70	9,000	50	7 Da.
5. Fibroid	Hysterectomy	160 M.	110/ 70	16,900	64	5 Da.

Comment

2. Temp. 99.2° Before Operation—Injury to Bladder.
4. Albumin in Urine—Fell Out of Bed 5th Day.
5. Albumin in Urine—Shock—Considerable Blood Lost at Operation.

TABLE VI.   PARALYTIC ILEUS—LOW GRADE PERITONITIS

DIAGNOSIS	OPERATION	TIME	B.P.	W.B.C.	PMN.	PRE-OP. T.	URINE	DIED DAY
1. Adenomyoma	Hyst., Bilat. S.O.	85	135/65	6,300	80	99.0°	Neg.	7th
2. Fibroid Cyst	Hyst., B.S.O., App.	80	116/66	13,500	65	99.8°	Neg.	4th
3. Lac., Retroversion	Plast., Susp., App.	75	100/66	9,400	80	99.0°	Sug.	6th
4. Cholecystitis	Cholecysteet., App.	60	105/70	10,200	62	99.4°	Trace alb.	7th

Comment

1. Highest Temperature P.O. 100.8°.
2. Pseudomucinous Cyst—Gastric Dilatation—Progressive Rise in Temp. to 101.8°.
3. Possible Intestinal Obstruction.
4. Extreme Exhaustion, Slow Pulse.
   All Cases—Low Temperature

Operation in the most skilled hands in the presence of an active infection is always dangerous and especially so when preceded by a prolonged period of septic absorption.   Table VII is self-explanatory.

TABLE VII.   PROLONGED SEPSIS—MAJOR OPERATION—SHOCK

DIAGNOSIS	OPERATION	TIME	W.B.C.	PMN.	PRE-OP. TEMP.	DIED
1. Tbc. Salpingitis	Hyst. Bilat. S. & O.	70 M.	16,800	80	99.0°	41 Hr.
2. Tbc. Salpingitis	Hyst. Bilat. S. & O.	60 M.	11,250	80	100.4°	41 Hr.
3. Ac. Purulent Salping.	Panhyst. Bi. S. & O.	105 M.	10,000	85	99.0°	87 Hr.
4. Postpart. Inf.	Part. Hyst., S. & O.	60 M.	15,200	88	103.4°	48 Hr.
5. Fib. Rad. Peritonitis	Cecostomy	70 M.	10,800	87	102.6°	14 Hr.

Comment

1. Posterior Colpotomy 25 Days Before.
2. Postoperative Sinus 6 Months.
   In all cases frank pus was found.

A detailed study of the Tables of the 16 patients who died from what we class as acute fulminating infection reveals the fact that in the preoperative record there is evidence of latent infection or potential infection with poor resistance shown by a leucocytosis or elevation of temperature or a leucopenia, or a low polynuclear count, and yet the significance of these findings was overlooked.   Furthermore, microscopical examination of the pathologic specimen removed from 12 of these women shows the cell changes of subacute inflammation or of recent activity in an old inflammatory process.

In contrast with this group there are 5 fatalities in which the symptoms and clinical picture is that of a definite spreading peritonitis.

In the last group we find 8 deaths due to paralytic ileus and a low grade peritonitis.   All of these had some suggestive danger signal in their preoperative record, yet it was passed over without comment.

Our experience in pelvic surgery has not been that late postoperative distention and vomiting is due to an actual obstruction or band constriction, but, rather, that it takes the form of partial obstruction; many times there is passage of gas by the rectum and even bowel

movement, but the vomiting continues and the gas quickly reaccumulates after an enema or lavage.

Reopening on autopsy has invariably revealed some loop of intestine slightly adherent to a point in the operative field or to the abdominal wound, slightly kinking the bowel lumen but not obstructing it. The pulse and temperature are not much elevated, yet regurgitant vomiting, distention, and gas pains persist. The vomiting quickly recurs after lavage.

High enterostomy under local anesthesia without disturbing the exudative process, near the operative field, will save many but it must be done early.

A review such as presented is a sad commentary on our surgical judgment and our surgical care, for even a casual study of the facts show that:

1. Not sufficient attention is given to the suggestive findings developed in our preoperative study.

2. That surgical judgment can only be developed by pathologic study of the living.

3. That the patient pays the cost of training men, for speed and technic are the products of training, and finally that such reviews are illuminating in that they reveal our errors.

20 LIVINGSTON STREET.

Books Received

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